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SERUM PROTEIN-BOUND IODINE CONCENTRATION IN BLOOD OF EUTHYROID MEN AGED 18 TO 94 YEARS*

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During the past several decades there have appeared numerous reports on the concentration of the protein-bound iodine in the blood plasma or serum of patients tested for reason of suspicion of thyroid dysfunction. Certain of these have included values obtained in patients who, in retrospect, demonstrated no clear-cut evidence of thyroid abnormality (6, 14, 24). Few reports, however, have included data on normal subjects for whom there was no clinical indication for study, and which also include information appropriate for statistical evaluation of the data (table 1) (4, 7, 11, 29, 42, 47, 51, 52, 53, 55) obtained by several methods (2, 3, 4, 11, 14, 15, 16, 17, 18, 37, 52, 54, 56). From the standpoint of comparing the distribution of values in some of the latter reports it is unfortunate that there is uncertainty as to whether the reported standard deviations are based on single or the mean of duplicate or triplicate determinations on each specimen.

While there have been reports on the accuracy of the determination based on reproducibility of results on duplicate determinations on the specimen obtained from each subject, or on replicate determinations of aliquots of a single pooled plasma, serum or standard (1, 13, 17, 23, 30, 40, 47, 49), we are not aware of any reports, including any substantial number of normal subjects, on the day-to-day or long-term, variability in values for the protein-bound iodine due to biological sources. Perusal of available reports on the relation of senescence in the human to the concentration of circulating thyroid hormone, as indicated by the plasma or serum protein-bound (8, 15, 25, 26, 27, 28, 38, 39, 41, 46, 50, 55) or butanol-extractable (26, 27, 36) iodine, moreover, leads to the inference that definitive evidence for correlation with age in the adult is scanty and uncertain. Accordingly, we have considered it worth while to report findings on the level of the protein-bound iodine in the serum or plasma in several groups of reasonably healthy young, middle-aged, and elderly men, for whom there was no reason for suspicion of thyroid disease on clinical grounds.

MATERIALS AND METHODS

Subjects

All of the 192 subjects included in the present study were ambulatory, apparently healthy men selected from the following groups:

Group A.—Six subjects, aged 27 to 50, were members of the staff of the Gerontology Branch.

Group B.—These 174 subjects, aged 40 to 94, were selected from the ward of the Division of Research Gerontology and Infirmary of the Baltimore City Hospitals. Further description of most of these men, and the criteria used in their selection are reported elsewhere (19).

Group C.—These 12 subjects, aged 18 to 27, were normal volunteers from the Clinical Center of the National Institutes of Health.

Experimental Procedure

Analytical Method 1.—Heparinized plasma specimens obtained without regard to alimentary state were analyzed in the laboratory of the Gerontology Branch according to the method of O'Neal and Simms (40), modified as follows (where the letters refer to steps in O'Neal and Simms' report): Precipitation of protein: (a) 1.0 ml. of plasma was assayed; (b) 15 ml. of

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15% tricholoroacetic acid were added; (c) the precipitate was washed with 15% trichloroacetic acid; (d) omitted. Digestion-oxidation: (a) 5.0 ml. of chloric acid were added to the washed precipitate; the tubes were places in a boiling water bath for 30 minutes to facilitate partial dissolution of the precipitate; 4 rinses, each with 3.0 ml. of chloric acid, were made (a total of 17.0 ml. of chloric acid were used for the digestion); (b) 0.5 ml. of chromic acid was added; (c) omitted. In the preparation of standards, the tubes contained 17 ml. of chloric acid and 0.5 ml. of chromic acid. Standards prepared daily contained 0.025, 0.050, 0.075, and 0.100 μg. of added iodate. Thus, the amounts of I in the 4.0 ml. aliquots (of the 5.0 ml. diluted digests) used for reading were, respectively 0.02, 0.04, 0.06, and 0.08 μg. Spectrophotometry: (a) 5.0 ml. of water were added to each tube; (e) at 1.0 minute intervals, the ceric ammonium sulfate solution was added to each of 4 tubes. After mixing, the tubes were returned immediately to the water bath; (f) A Beckman Model DU spectrophotometer was used, and readings were made at 1.0 minute intervals. Thus each tube was read every 4 minutes.

Analytical Method 2.—Serum was obtained in the fasting state and was analyzed in duplicate in the laboratory of the Gerontology Branch. Except where specifically noted to the contrary, the value reported is the mean of the duplicate determinations. The method used was that of Barker, Humphrey, and Soley (4) with several minor changes in procedure. To minimize iodine contamination, concentrated hydrochloric acid and sulfuric acid solutions were boiled for 45 minutes and then restored to original volumes with triple distilled water prior to use in the preparation of the stock solutions. The concentration of the ceric ammonium sulfate solution was selected on the basis of transmittance readings, following others (10, 22). The standard solutions contained 0.02, 0.04, 0.06, and 0.08 μg. I per ml. After mixing, a 4 ml. aliquot was taken.

For the colorimetric determination of unknowns, a 4 ml. aliquot of the supernatant was used. One ml. of the stock solution of ceric ammonium sulfate was added to each tube. Readings were made at 0 minutes, as well as 6 and 12 minutes, using a Beckman Model DU Spectrophotometer at 420 mμ.

In the preparation of standard curves, several features of the modification by Ware, Grillhoesl, and Grant (pp. 22-30 of reference 50) have been utilized. Six- and 12-minute standard curves were constructed on ordinary graph paper by plotting percentage transmittance readings of the reagent blank and of each of the iodide standards against the concentration of the iodide. All of the points on each curve fell on a straight line, which intersected the abscissa at a point above the zero-time percentage transmittance reading. Since the zero-time readings of all samples were approximately the same (a further check on accuracy), a mean was used. The distance between the point of intersection and the zero-time percentage transmittance reading was considered to represent the decolorization due to the iodide in the reagent blank. To compensate for the iodine in the reagent blank, all readings were moved down vertically on the chart—a distance equal to that between the zero-time reading and the

TABLE 1. PROTEIN-BOUND IODINE IN BLOOD SERUM OR PLASMA OF NORMAL ADULT HUMAN SUBJECTS.

Author (Reference)	Method (Reference)	N	Protein-bound Iodine (μg./100 ml.)	
			Mean	S. D.*
Barker, Humphrey, and Soley (4)	Barker, Humphrey, and Soley (4)	68	5.1	1.0
Bodansky, Benua, and Pennachia (7)	Zak and associates (56), modified	100	6.2	1.3
Campos and associates (11)	Barker, Humphrey, and Soley (4)	85	6.9	1.4
Kydd, Man, and Peters (29)	Man and associates (37), modified	80	5.4	0.9
Perry and Cosgrove (42)	Taurog and Chaikoff (54)	34	5.9	1.3
Skanske and Hedenskog (47)	Barker, Humphrey, and Soley (4), modified	100	5.9	0.7
Strickland and Maloney (52)	Strickland and Maloney (52)	25	5.5	0.9
Sunderman and Sunderman (53)	Barker and Humphrey (3)	65	5.0	1.0
Tucker and Keys (55)	Barker (2), modified	402	5.8	1.3
Present study	O'Neal and Simms (40)	72	6.6	1.2
	Barker, Humphrey, and Soley (4), Bio-Science Lab.	124	5.5	0.9
	Barker, Humphrey, and Soley (4), modified	101	5.0	0.9

* Standard deviation of the mean.

reading of the reagent blank at 6 minutes and at 12 minutes. A straight line was then drawn through the points on each curve corrected for the reagent blank. The two new curves intersected the abscissa at the zero-point reading. The original points were erased, and the unknown values (including reagent blank) were read from their respective curves. The iodide concentration of the reagent blank was then subtracted from the values obtained for each unknown sample. A mean of the 6- and 12-minute values was taken to obtain the final result.

Analytical Method 3.—Serum was obtained in the fasting state and, identified only by code number, was sent to the Bio-Science Laboratories at Los Angeles, California, for assay. Each sample was analyzed in duplicate. The results for both determinations were made available to us and, except where specifically noted otherwise, the mean of these values is presented in this report. The determinations were done by the alkaline ashing method of Barker, Humphrey, and Soley (4), modified as follows: Protein precipitation of 1 ml. aliquot in duplicate was carried out using Somogyi's reagents, followed by two washes of the precipitate. The supernatant from the initial precipitation was used to check for excessive inorganic iodine. Samples manifesting a high inorganic iodine-level were rechecked after washing the precipitate. To the washed precipitate was added 0.5 ml. of 4N Na_2CO_3 (half the volume used in the original method). The tubes were then dried in electrical heating blocks at about 100 C. Incineration was carried out at 600 C. for 30 minutes (the latter conditions a variation from the procedure described by Barker, Humphrey, and Soley, were found adequate in a time and temperature study of the incineration step). The ash was dissolved in an acid mixture containing sodium arsenite, water was added, and the mixture was stirred and centrifuged. Five ml. were taken for colorimetry with ceric ammonium sulfate, the reaction taking place at 37 C. for 20 minutes. It was found necessary to check for Tyndall effect in the solutions in the tubes before adding the ceric ammonium sulfate.

Each incineration included a pooled serum standard in duplicate and an absolute standard of KI in duplicate. The latter standard was fully recoverable if a solution of gamma globulin was included from the beginning as a carrier. Bovine gamma globulin, used for this purpose, added a blank of about 0.4-0.7 μg. per 100 ml., each batch being tested before use. Standard curves of 5 points were run once or twice daily. Recoveries were so close to 100% that no correction was made for loss of iodine. The above-described modification used at Bio-Science Laboratories, based on the experience at the latter laboratory, gives results about 0.5 μg. % higher on the average than those given by the original method.

For the purpose of estimating variability due to technical sources, the results of duplicate analyses on samples analyzed at Bio-Science Laboratories and in the laboratory of the Gerontology Branch by the modified Barker method were used. In addition, 18 aliquots of the same pooled sera specimen were sent to the Bio-Science Laboratories for assay. These were included in 5 shipments sent over a 6-month period. These samples were identified to the analyst only by their different code numbers, which could not be distinguished from those assigned to other specimens included in the same shipment. All analyses were carried out in duplicate. To estimate variability due to the sum of technical and individual biological sources, tests on 72 subjects were repeated after intervals of one day to 7 months.

Statistical methods employed were as described by Snedecor (48).

RESULTS

Analysis of Variance

Variability due to technique.—For duplicate determinations on 148 sera in the laboratory of the Gerontology Branch (Barker, Method 2), the sample mean difference was 0.129 μg. per 100 ml., sample standard deviation of the differences was 0.376 μg. per 100 ml. and sample standard error of the mean difference was 0.031 μg. per 100 ml. For duplicate determinations on sera at the Bio-Science Laboratories, the corresponding findings were 0.022, 0.263 and 0.017 μg. per 100 ml., respectively. For determinations carried out over a period of 6 months in duplicate on 18 aliquots of the same pooled sera specimen, values ranged from 5.2 to 6.3 μg. per 100 ml. The mean value, sample standard deviation and coefficient of variation for these determinations were 5.78, 0.30 μg. per 100 ml., and 5.2%, respectively. These values are in agreement with variability due to technical sources reported by others using similar

(1, 12, 23, 47) or somewhat different techniques (6, 13, 17, 20, 40, 43, 45, 49) and indicate a probable analytical error of approximately ± 0.3 to ± 0.4 μg. per 100 ml.

Biological variation.—Day-to-day variation in the PBI content of plasma or serum was estimated from determinations made on the same subject at intervals of one day to 7 months. Results are summarized in the upper section of table 2. Reliability coefficients (correlation between tests on same subjects on two different days) ranged from 0.34 to 0.62, depending on the analytical method used. The standard errors of estimate ranged from 1.23 to 0.62 μg./100 ml. Using analytical method 1, there was no indication that increasing the time interval between successive tests reduced the correlation coefficient. It is clear that among euthyroid subjects the PBI shows a high degree of biological variation and does not sharply differentiate between individuals.

Regression on age.—The regression of PBI levels on age is shown in figure 1. In order to eliminate the variance introduced because of systematic differences in the analytical methods, the data are presented according to the method used (A, B, and C). Frequency distributions are shown at the right of each curve. There is no indication of excessive skewness in these distributions. The correlation with age is insignificant (table 2). Hence, mean values for the entire group have been calculated for each analytical method (table 2). O'Neal and Simms give higher values (mean 6.55 ± 1.2 μg./100 ml.) than the Barker method (means 4.97 ± 0.87 and 5.53 ± 0.90 μg./100 ml.).

DISCUSSION

Systematic Differences Associated with Technique

The difference in results obtained by the two modifications of the alkaline ashing method of Barker, Humphrey, and Soley has been noted above under Methods. This is further substantiated by comparison of results obtained by assay of each of 141 serum specimens from normal subjects by both techniques. The average difference in results obtained by the two modifications was 0.48 μg. per 100 ml. The standard deviation of the differences was 0.77 μg. per 100 ml., and the standard error of the difference was 0.065 μg. per 100 ml. This difference is highly significant ($P < 0.001$). The difference between the results by the alkaline ashing procedure of Barker, Humphrey, and Soley and the chloric method of O'Neal and Simms has been clearly demonstrated by Zieve, Dahle, and Schultz (57), who analyzed samples for 50 euthyroid individuals by both procedures in agreement with our results. They

TABLE 2. DAY-TO-DAY VARIATION IN PROTEIN-BOUND IODINE (PBI) AND CHANGES WITH AGE.

	Method of Analysis		
	Method 1 O'Neal and Simms (Gerontology Branch)	Method 2 Barker, Humphrey, and Soley (Gerontology Branch)	Method 3 Barker, Humphrey, and Soley (Bio-Science Laboratories)
Material Examined	Plasma	Serum	Serum
N	29	21	37
Interval (days)	13–210	30–150	30–150
r	.41	0.62	0.36
σ Estimate (μg./100 ml.)	1.13	0.62	0.86
Material Examined	Plasma	Serum	Serum
N	64	——	——
Interval (days)	1–13	——	——
r	0.34	——	——
σ Estimate (μg./100 ml.)	1.23	——	——
	Age Changes		
Material Examined	Plasma	Serum	Serum
Age range (years)	18–91	27–89	27–94
Mean age (years)	60.8	67.8	69.3
N	72	101	124
r (PBI vs. age)	−0.08*	−0.01*	−0.06*
Mean value (μg./100 ml.)	6.55	4.97	5.53
Standard deviation (μg./100 ml.) of the mean	1.2	0.87	0.90

* Not significant.

obtained values in the incineration and chloric acid techniques of 5.4 and 6.7 μg. per 100 ml., respectively. The difference in results by the two methods was highly significant. From the cumulative frequency distributions these workers concluded that "it is clear that the entire distribution of euthyroid values obtained with the chloric acid method has been shifted upward by approximately 1 to 1.5 μg. per cent."

Relation of the Level of the Circulating PBI to Age

Kountz, Chieffi, and Kirk (28) concluded, from their data on protein-bound iodine in the blood of 78 men (25 to more than 80 years old), that there was a decrease with increasing age. By results of analysis of variance of their data ($F = 2.69$, 4 degrees of freedom for means for age decades and 73 degrees of freedom for individuals in decade age groups), it was found that the regression of the mean values for the serum protein-bound iodine on age was significant at only the 5% level.

In a study by Tucker and Keys (55), the difference between the mean value obtained for the young men (ages 18-25, mean 6.25, S.D. 1.46 μg./100 ml.) differed from the mean value obtained for middle-aged men (ages 45-56, mean 5.63, S.D. 1.21 μg./100 ml.) at a level of statistical significance within 1%. The present series does not include a large enough sample of subjects in the age groups, 18-25 years, to make a direct comparison. However, there is no indication in our data of a significant difference between subjects aged 45-55 years and those 56-95 years, although the mean value for the total group is lower than that reported by Tucker and Keys (55). Scazziga, Barbieri, and Beraud (46) have reported markedly increased values for PBI in a small sample of senile subjects. We can only say that these results are at variance to our own and many other studies.

For the most part, previous studies have failed to demonstrate any relationship between PBI levels in the blood and age, although the data offered are too scanty for statistical evaluation. Thus, in a group of 313 persons composed of a few volunteers and a large proportion of euthyroid patients (63 men and 25 women), Dailey and Skahan (14) found no relation between age and the level of the protein-bound iodine ($r = -0.10$).

Numerous investigators have commented on the stability of PBI measurements over the life

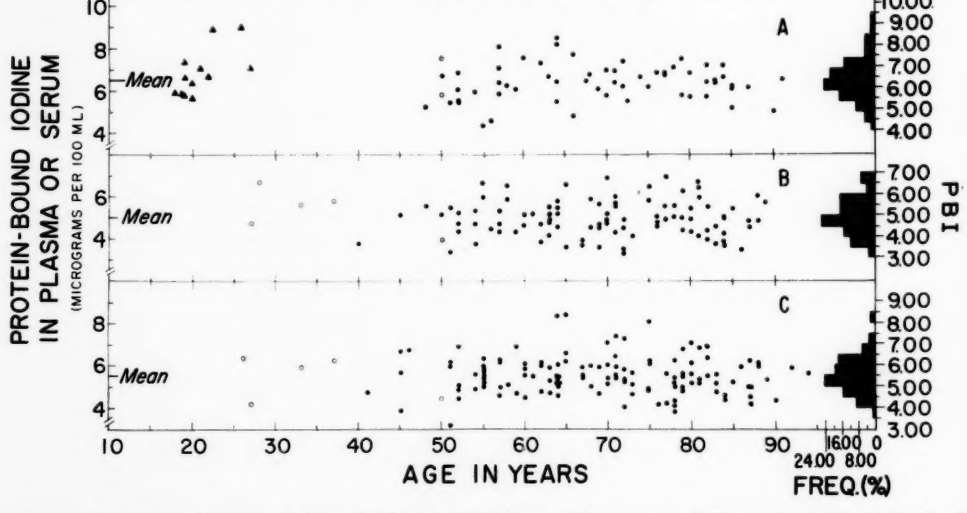

Fig. 1. Regression of serum or plasma levels of protein-bound iodine on age. A. Determinations by O'Neal and Simms' method (Group A-O) (40). B. Determinations by modified Barker, Humphrey, and Soley's method (Group B-▲) (4) by Gerontology Branch. C. Determinations by modified Barker, Humphrey, and Soley's method (Group C-●) (4) by Bio-Science Laboratories. Frequency distributions are shown at the right of the figure.

span, but data for a critical evaluation of the question have been lacking (16, 36). Klein (26, 27) presents only the mean values for protein-bound iodine, and butanol-extractable iodine groups arranged according to age decades. These values remain fairly stable with increasing age. Values for protein-bound iodine parallel those for the butanol-extractable iodine in agreement with others (6, 9). The mean value of a group of 28 patients without evidence of thyroid disease, who were 75 years old or older, was not significantly different from that of 100 normal adults collected by Starr and his associates (51). The data of Soley and Humphrey, presented by Starr (50), were apparently obtained on patients for whom there was indication for determinations of PBI for diagnostic purposes. Their use for gerontological and physiological purposes, accordingly, is somewhat suspect. Perlmutter and Riggs (41) reported individual values for serum protein-bound iodine for 17 euthyroid patients of ages 28-70, as did Perry and Cosgrove (42) for 34 normal adults of ages 16 to 64. No diminution in the values was noted with increasing age. While Bonate, Salvi and Rancati (8) concluded, from their data on 13 normal subjects of ages 65-70, that the protein-bound iodine was lower than in young subjects, their study, unfortunately, included no young controls. The finding by Mezzasalma, Mars, and Morpurgo (39) that there was no age difference when the protein-bound iodine in young subjects was compared with that in a group of old arteriosclerotic patients was based on a small number of normal subjects (N = 23) who showed very wide individual differences.

The results obtained in the present study, finally, do not suggest a regression on age in the level of the serum or plasma protein-bound iodine, at least over the age span of 50 to 95 years. In view of the limitations in the reliability of the measurement of protein-bound iodine in subjects drawn entirely from the normal euthyroid range of function (see table 2), it cannot be concluded that regression on age has been ruled out. It is also possible that young adults (aged 18-25 years) have, on the average, slightly higher levels of PBI than do middle-aged or elderly adults. We can say, with assurance, that there is no systematic reduction in PBI levels after the age of 50.

Physiologic Significance of the Stability of the Level of the Circulating Thyroid Hormone with Increasing Age

The relative constancy in the level of the protein-bound iodine in the serum or plasma with increasing age should not be interpreted to indicate that there is no change (or, at the most, only slight change) with increasing age, in the rate of its secretion of its hormone by the thyroid gland. Although there is, in a total distribution including hypo- and hyperthyroid subjects, correlation between the level of the PBI and the basal metabolic rate (4, 5, 16, 23, 31, 32, 33, 34, 42, 44) and between the level of the PBI and clinical disease state (4, 6, 35), there exists no evidence that, for individuals within the normal euthyroid range of function, the level of PBI, as measured by available techniques, can be used to detect individual differences in the rate of secretion of its hormone by the thyroid gland (18, 21).

SUMMARY

In 192 healthy men, aged 18-94 years, protein-bound iodine in blood plasma or serum was estimated by modifications of alkaline ashing (Barker, Humphrey, and Soley) or chloric acid methods (O'Neal and Simms).

The findings of the present study and other available evidence do not support the proposition that there is alteration of the level of PBI with increasing age.

Sources of variance in the results were investigated by duplicate determinations on specimens, repeated determinations on a pooled specimen, and by repeating the determination one or more times in selected subjects on specimens drawn after an interval of one day to 7 months. The data lead to the inference that within individuals the variability due to biological sources (0.6-1.2 μg./100 ml.) is larger than that due to technical analytical sources (0.3-0.4 μg./100 ml.). Increase in the interval between tests (from 1-13 days to 13 days-7 months) did not increase the standard error of measurement. The mean value for all subjects by the chloric acid method was 6.55 ± 1.2 μg./100 ml. and for the alkaline ashing method 4.97 ± 0.87 and 5.53 ± 0.90 from two different laboratories.

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MATERNAL AGE, POLYDACTYLISM, AND LITTER SIZE IN MICE

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Parental age at the time of conception has been reported to have variable to negative effects on the transmissibility of certain phenotypic characteristics in animals. Wright (11) has shown in guinea pigs and also Holt (5) in mice that parental age is the most important factor influencing the penetrance of polydactylism in these mammals. Wright's analysis further demonstrated that this age-dependent characteristic was altered more severely by the maternal rather than paternal aging process. Wright attributed this maternal age effect on this characteristic as being sensitive to aging and due to immaturity rather than to a senescent effect. On the other hand, Chase (2) found that maternal age had an insignificant effect on the penetrance of polydactylism in mice. Those reports which show that polydactylism is age-dependent suggest that some principle, presumably of maternal origin, is producing alterations in the germ cells which are transmitted to the offspring.

Since this complex phenotypic characteristic apparently responds differently to the aging process, this experiment was designed to show whether age alone or age combined with parity produces significant variability in the occurrence of polydactylism and litter size in this polydactylous strain of mice.

Litter size, the number of young born either dead or alive, is not a simple characteristic but is dependent on at least several variables: fecundity, number of eggs fertilized, and prenatal mortality. Fecundity, the number of eggs liberated by the ovaries at ovulation, is the upper limiting factor for litter size. The number of eggs ovulated, as measured by the number of corpora lutea, has been found to increase with parity, the number of times the mother has born a litter, and maternal age (7). Murray (8) reports parity (litter seriation) as a more important factor in the reduction of litter size than maternal age.

MATERIALS AND METHODS

All mice used in this investigation were selected from the F23 - F30 generations of a polydactylous strain of mice maintained at the Springville Biological Station. The origin and method of propagation of this strain of mice were reported previously (10). To minimize any possible parental age influence between different maternal age descents, mice were selected from the $<$ 100-day descent only (3). This $<$ 100-day maternal age descent of mice from the F23 - F30 generations has reached the 92% penetrance level for polydactylism.

For the present study, mice were weaned at ages between 28-32 days, divided by sex, and separated for periods of 1-38 weeks, the separation period computed from the time of weaning to the time these mice were mated together. The data obtained from the breeding of these virgin mice were restricted to their first litters only. The controls, mice mated at weaning age, were selected from the same generations and maternal age group as were the present experimental animals. To make the comparison in both groups with respect to maternal age, grouping of litters born to females of the control group resulted in slight overlapping in litter seriation due to differences in the fecundity of the different female mice used.

A total of 3140 newborn mice (1340 control; 1800 experimental) were classified on the day of birth and records kept of the days the parents were born, weaned, mated, litters born, and number of stillbirths. In the experimental group, mice which had difficult parturition (which increased with the prolonged delayed matings) were killed and the young were removed from the uterus and classified. This procedure reduced the number of unclassifiable young (as to polydactylism) but also increased the number of young observed in the last age group as compared to the number of young born in the controls of the same maternal age.

The data of this experiment were susceptible to many-sided analysis. Consideration was given only to those relating penetrance of polydactylism and litter size to age, and to age and

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parity combined. The material on fecundity, fertility, and newborn mortality is not discussed.

Dietary requirements, laboratory physical conditions, and other maintenance details were kept uniform throughout the periods covered.

RESULTS

The data on penetrance of polydactylism in mice of the < 100-day maternal age descent from F23 - F30 generations are shown in table 1. These data are composed of 1800 experimental mice and 1340 mice in the control group. The mean penetrance values for the experimental and control groups was 96.0 ± 2.6% and 94.4 ± 1.6%, respectively. The difference in the means is 1.6%, which is found to be insignificant at the 95% level. These results justify the conclusion that neither age nor age and parity combined significantly alter the occurrence of polydactylism in the offspring.

The data representing litter size in the experimental and control groups of mice were analyzed with respect to mean litter size, standard deviation, and coefficient of variability in table 2 and as changes in the coefficient of variability (△c) in table 2 and figure 1. In both groups of mice the maximum mean litter size (experimental, 6.0 ± 4.0; control, 6.9 ± 3.8) was born to females of the 101-200-day-old group. The minimum mean litter size was born to females of the 301-400-day-age group (experimental, 4.7 ± 3.6; control, 3.7 ± 3.8). Females in the 201-300-day-age group showed the highest degree of variability in litter size. Intragroup comparison of the standard error of the difference between means was found to be significant at the 95% level only between the 301-400-day-age group. However, this difference is due mainly to the method (young were removed from the uteri in the experimental group) rather than to the period the mice were separated prior to mating.

In figure 1 the change in coefficient of variability (△c) is plotted against maternal age. It is seen from this figure that the rate of variability in litter size in the two groups of mice differs slightly. In mice mated at weaning age, the change in variability of mice 0-200 days old was found to be +8 as compared to a value of

TABLE 1. THE PENETRANCE OF POLYDACTYLISM IN INBRED MICE OF TWO GROUPS, CONTROL (MICE MATED AT WEANING) AND EXPERIMENTAL (SEXES SEPARATED AND MATING DELAYED) AS MEASURED BY MATERNAL AGE. THE PARENTAL ANCESTORS OF THESE MICE WERE FROM THE <100 DAY MATERNAL AGE DESCENT OF THE F23 - F30 GENERATIONS.

Class Interval (Days)	Mean Female Age (Days)	Polydactylism (%)
0 -100		
Control	79	95.5
Experimental	85	95.3
101-200		
Control	152	94.0
Experimental	143	97.9
201-300		
Control	252	93.4
Experimental	240	96.3
301-400		
Control	349	94.8
Experimental	323	94.3

TABLE 2. MEAN LITTER SIZE IN INBRED POLYDACTYLOUS MICE AS MEASURED BY MATERNAL AGE IN TWO GROUPS, CONTROL (MICE MATED AT WEANING) AND EXPERIMENTAL (SEXES SEPARATED AT WEANING AND MATING DELAYED) IN THE <100 DAY MATERNAL AGE DESCENT OF THE F23 - F30 GENERATIONS.

Class Interval	Mean Age of Female (Days)	Mean Litter Size	Litter 2 Standard Deviations	Coefficient of Variation	△ C
Control					
0-100	79	6.2	±4.4	35.5	——
101-200	152	6.9	±3.8	27.5	+ 8
201-300	252	5.5	±5.4	49.1	−21.6
301-400	349	3.7	±3.8	51.4	− 2.3
Experimental					
0-100	85	5.9	±4.2	35.6	——
101-200	143	6.0	±4.0	33.0	+ 2.6
201-300	240	5.6	±5.4	48.2	−15.2
301-400	323	4.7	±3.6	38.3	+ 9.9

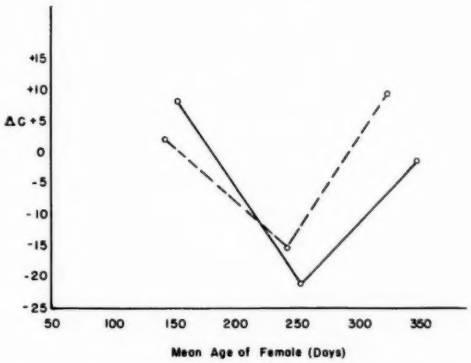

Fig. 1. Change in coefficient of variation (Y-axis) plotted against the mean age of females (X-axis) for the control, (solid line) and the experimental groups (dash line).

+2.6 for mice of the experimental group. The change in variability of mice in the 101-300-day-age group was found to be greater in the control (−21.6) than in the experimental group (−15.6). Finally a divergent trend is observed in the change of variability in mice of the 201-400-age group. The magnitude of change in the variability in the 201-400-day-age group of the experimental group is approximately the same as in the 0-200-day-age group of the control. It is of interest to note that the inflexion point in ($\triangle$c), which occurs at approximately 250 days, remains fixed regardless of the previous sexual experiences of these mice.

DISCUSSION

All fluctuations in mammalian phenotypes as measured by maternal age which have been reported have at least one feature in common—they are under the control of complex genetic modifying factors (4, 5, 9).

The data representing penetrance of polydactylism (table 1) in offspring of control and experimental groups justify the conclusion that in the first reproductive year of a mouse insignificant differences are found in the percentage of polydactylous offspring born to parents aged prior to mating or to females having young while aging. These data tentatively suggest the possibility that if aging does reduce the occurrence of polydactylism in offspring born to aging parents, the process must be accumulative and proceeds at a very slow rate.

In a polydactylous descent of mice, Chase (2) found no significant change in the frequency of polydactylous offspring as females aged. Holt (5) (in mice) and Wright (11) (in guinea pigs) reported a decrease in this characteristic as maternal age increases. This comparative variability observed in the penetrance of polydactylism as measured by maternal age suggests that this characteristic may be of different types as Landauer (6) reports in fowl. If this is found to be the case in mice, then it is also possible that polydactylism in mice is influenced by different but interrelated genetic complexes, each of which may respond differently to maternal age effects.

The data on litter size show that litter size in both groups of mice decreases as females age. These data also show that aging prior to mating does not significantly decrease litter size of comparable age groups. Murray (8) and Bittner (1) have obtained identical trends in mice mated throughout their reproductive life span. These data do show that the rate of change in the ability of females to have young proceeds at slightly different rates, while the maximum change in variability occurs at approximately 250 days in both groups of mice.

From our data on mean litter size (table 2) and the graphical representation of these data in figure 1, three phases in the reproductive life span of mice, regardless of previous sexual experience, can be distinguished: the period of early sexual immaturity represented by mice less than 100 days old; the period of sexual maturity (mice approximately 101-250 days old); and finally the period after 250 days, where aging effects on the reproductive capacity gradually decrease and also become sporadic. The comparable trends and inflexion point, which occurs at approximately 250 days (fig. 1), suggest that litter size in both groups of mice is influenced by the same intrinsic and/or extrinsic factors which regulate the number of young born.

SUMMARY

Parent aging effect on polydactylism and litter size has been investigated in the F23 - F30 generations of inbred mice. The mice utilized in this experiment were born to parents which were < 100 days old and had reached the 92% level for polydactylism.

Data on the effects of aging were obtained under two conditions: mice mated at weaning time and remaining together throughout their reproductive span (controls), and mice mated after being separated from 1-38 weeks.

The data show that parental age insignificantly influenced the transmissibility of polydactylism to either group of mice (the average for the control group was 94.4 ± 1.6% and the experimental group, 96.0 ± 2.6%).

Litter size decreased with maternal age within both groups of mice (control, 6.2 - 3.7; experimental, 5.9 - 4.7). Intergroup differences show a slight but insignificant reduction in litter size as compared to maternal age. In both the experimental and control mice maximum variability occurred when mice were 201-300 days of age. Minimum variability in litter size was found within the same two age groups (101-200 and 301-400-day-old females) of both the experimental and control groups. It seems that the peak of sexual reproductivity occurred when these mice were approximately 250 days of age. It can be concluded that neither inbreeding,

age of parent when the first litter was born, nor aging and having young had little if any effect on litter size. What determines litter size therefore must be of a different nature.

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VARIATION IN GESTATION LENGTH AND LITTER SIZE OF THE GOLDEN HAMSTER, MESOCRICETUS AURATUS*

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Variation in gestation time correlated with advanced age has been reported for several species. Asdell (1) noted a two-day extension from the normal for the 8-year-old ewe and over one day in the 6-year-old goat. For sheep, Terrill and Hazel (19) observed an average increase of 0.27 day for each advancing year of age. Brakel and associates (6) found that the mean gestation length of cows 5 years old and over significantly exceeded that of two-year-old cows by 1.5 days. Knoop and Hayden (10) suggested a slight increase with age of the cow up to 6 years, perhaps 2.5 days in all.

Many investigations have described the changes accompanying aging in mammals. Classical work in this field includes that of Rolle and Charipper (16), who reported the progressive invasion by fibrous connective tissue of the ovary of aging female hamsters. Spagnoli and Charipper (18) also observed definite alteration of cellular structure, vacuolization, and degranulation of anterior pituitary cells in the aging male and female hamsters. Bond (5) suggested that the active reproductive life of the female hamster is limited to the first 11 months.

Physiological factors related to this apparent reduction of reproductive ability in older females may include loss of tissue and organ sensitivity to the anterior pituitary secretions (15), loss of ovarian function because of invasion by connective tissue (16), and progressive hormonal imbalance of several organs (15). It is possible that any one or all of these factors contribute to reduction in the reproductive performance of older animals. This study presents evidence that delivery of reduced litter sizes by aged animals need not reflect a reduction in total number of ova released, fertilized, or implanted.

PROCEDURE

Mature female hamsters of all ages display a behavioral heat response similar to that described for the guinea pig (21) and the albino rat (3). Lordosis typically occurs at 4 days but occasionally at 5-day intervals. Although the heat response persists for an average of 18 hours (range 12-23) (4), ovulation occurs within 8 hours after the initiation of heat.

The hamsters used here were of inbred stock and were maintained on a complete rat ration chow in addition to lettuce and water. The animal room and laboratory were temperature-controlled with adequate light and air circulation. Routine observations were made on each female for each cycle and the initiation of the lordosis response. Matings were made within 4 hours of expected ovulation time to insure uniform timing of fertilization.

Due to the early sexual maturation of this species (28 days) (17), animals were checked from the age of three weeks for heat response and mated. Accurate accounts were made of delivery times and number in each litter. This procedure was followed throughout the expected life span of the species, 24.5 months (2).

RESULTS

Over a period of two years, a series of 186 dated matings and deliveries was obtained (table 1). Eleven one-month-old female hamsters were successfully bred. These delivered an average of 6.8 young per litter (range 2-11). The succeeding age groups through 13 months gave average litter sizes ranging from 6.4 at 5 months to 9.0 at 10 months. Figure 1 presents female animal ages at breeding with mean gestation length and litter sizes.

A chi-square test applied to litter sizes of females one through 13 months of age revealed no significant difference. From 14 to 26 months of age the number of successful matings de-

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clined and litter sizes were reduced. Of 12, 14-month-old females mated successfully, the average litter was 3.8, and for ages beyond 14 months, the average was two for months 16 and 22 while a single young was delivered for months 19, 22, 23, and 25.

Figure 2 shows the length of gestation for the hamsters of progressive ages. These are the same animals described in figure 1. The increase in gestation length correlated with the advancing age of the mother is highly significant as indicated with a t of 18.7 and a P of less than .001.

The earliest record of birth in young female hamsters has been reported (17) as 28 days at coitus. Although the normal length of gestation is generally stated to be 16 days (384 hours), there is a progressive extension of this period as age increases. The average length of gestation from months one through 5 is shorter than the assumed 16 days. Eleven females, 12 to 23 months of age, had deliveries at 17 days (408 hours) or longer.

TABLE 1. FEMALE HAMSTER AGE, NUMBER OF MATINGS, NUMBER OF PREGNANCIES, MEAN GESTATION LENGTHS, AND MEAN LITTER SIZES.

Age (Months)	No. of Matings	No. of Pregnancies	Mean Gestation Length (Hours)	Mean Litter Size
1	12	11	373	6.8
2	18	16	375	7.9
3	25	18	378	6.8
4	23	15	378	8.0
5	9	5	381	6.4
6	13	7	385	7.4
7	15	11	382	8.0
8	14	9	386	8.3
9	14	7	385	7.0
10	10	9	388	9.0
11	11	10	387	7.1
12	32	28	393	7.7
13	24	15	393	6.9
14	20	12	402	3.8
15	29	0	0	0
16	21	1	397	2.0
17	8	0	0	0
18	16	5	399	3.0
19	20	1	400	1.0
20	5	0	0	0
21	5	3	406	2.3
22	17	1	443	2.0
23	6	1	411	1.0
24	4	0	0	0
25	3	1	398	1.0
26	2	0	0	0
27	6	0	0	0
	376	186		

DISCUSSION

Many factors may affect the gestation period. Among these are genetic background, seasonal variations, and other internal and external environments. The actual provocative stimulus resulting in parturition has been suggested to be pressure, hormonal withdrawal, and secretion of other endocrine factors. It has been demonstrated by Hamilton and Hamilton (7) and Kirk (9) for the human and Loeb (13) for the mouse that a definite decrease in the urinary or plasma ketosteroid hormone content occurs with advancing age. Furthermore, replacements with supplementary progesterone, estrogen, or thyroid hormones have reversed such senile changes, at least to a degree (11). Histological involution was arrested with mitotic activity and tissue weight increase resulting.

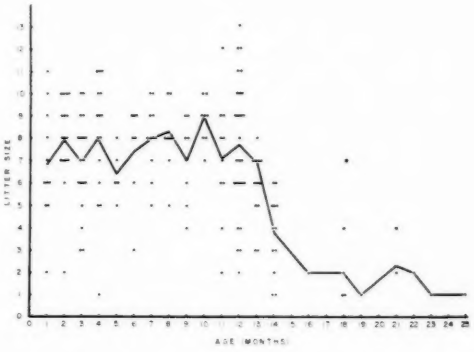

Fig. 1. Litter sizes from female hamsters one through 25 months of age.

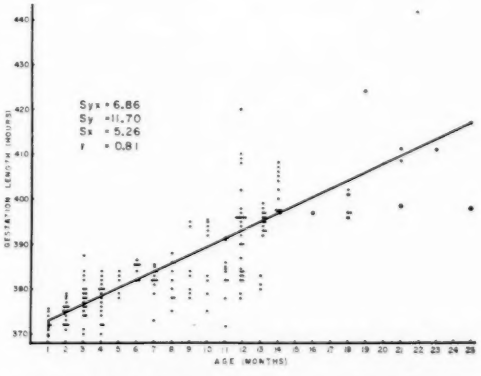

Fig. 2. Length of gestation for female hamsters one through 25 months of age.

Since pituitary gonadotropins increase with age, a possible cause of reduced ova production and release is loss of responsiveness to pituitary hormone stimulation. This has been suggested in the case of human menopause (8) and for the female rat (12).

Sections of senescent female hamster ovaries and uteri reveal no significant decrease in number of mature follicles or reduction in implantation sites. This suggests that among the older females, during the later stages of pregnancy, either the uterine tissues or placental nutrition is inadequate for continuation of pregnancy to term. During gestation in the majority of the older female hamsters, there is a continual rise in weight until the last two or three days of gestation, at which time there is a sudden drop in weight. Some evidence indicated that following a reduced vitamin intake, resorption or abortions increase (14, 20). It is suggested that a similar situation may be obtained within the aged animal and result in resorptions.

SUMMARY

Dated matings were made of 186 female golden hamsters, ranging in age from one month through 25 months. Data were collected and analyzed on the number in each litter and the length of gestation. Litter sizes from mothers aged one through 13 months were not significantly different. Fourteen months and beyond, the litter sizes were greatly reduced. The length of gestation showed a statistically significant increase as age increased. The reduced number in litters of senescent females is not the result of number of ova released and fertilized. Resorption in late gestation is the cause of smaller litter size.

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CHANGES IN RAT CARTILAGE MUCOPOLYSACCHARIDE WITH AGE AND RADIATION

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It has been observed that the mucopolysaccharide (MPS) composition of human and guinea pig cartilage changes with age. Haas (5) reported an increase of chondroitin sulfate (CSA), an acid mucopolysaccharide, in man from infancy to about age 40 and a decrease in later life. Other authors (8, 11), however, subsequently found a decrease in CSA with age from the highest value in fetal cartilage. In addition, the presence of hexosamine in excess of that required to combine with the uronic acid of CSA indicated the existence in cartilage of neutral polysaccharides also; the latter increased during the period of maturation and then remained constant through the remainder of life (6, 11). This non-CSA hexosamine was identified as glucosamine; mannose, galactose, fucose, and glucose were also found in hydrolyzates of human cartilage, suggesting that keratosulfate might be a component of this tissue (12). Keratosulfate was then isolated from young adult cartilage (9) and was later found to increase linearly during youth to a plateau at 20 to 30 years of age, which was maintained through the rest of the life span (7).

The acid polysaccharide and neutral polysaccharide of guinea pig cartilage also decreased markedly with age in relation to the dry weight of cartilage or to milligrams of carbon. This indicated a real decrease of MPS in spite of an increase in protein within the organic matrix and progressive mineralization of the tissue (3).

Since radiation hastens the appearance of various changes associated with aging (13), investigation into the effect of X irradiation as well as of age on changes in costal cartilage of rats was undertaken in this study.

MATERIALS AND METHODS

Male Sprague-Dawley rats 58 or 69 days of age were irradiated with 100, 300, 750, 850, or 900 r of X rays to the whole body. Radiation was administered with a 250-kvp G. E. Maxitron machine at a setting of 30 ma. with 0.1 mm. inherent and 3 mm. added Al filtration, a half-value layer of 0.4 mm. of Cu, and a dose rate of 55 or 80 r/minute. The $LD_{50}/30$ days of X rays for these rats was about 850 r. The animals were killed approximately 6, 9, and 12 months after irradiation, along with age controls kept under the same conditions, and costal cartilages removed. Cartilage of unirradiated rats of several other ages between 56 days and 2 years was also examined. Before they were killed the rats were starved for 16 hours, then injected either intraperitoneally or intravenously with 1.0 to 2.7 μc. of $Na_2S^{35}O_4$ in water per gram of body weight, put back on food and water, and finally killed 24 hours after injection. Cartilage was removed and stored at −62 C. until used. The cartilage was then freed from all other tissues (including perichondrium), finely chopped, dried in a vacuum oven at 58 C., and ground to pass through a 60-mesh screen. Fifty- or 100-mg. samples of cartilage were treated with 3 ml. of a 0.1% trypsin* solution in 0.1 M $NaHCO_3$ buffer (pH 8.2, 0.001 M with respect to $CaCl_2$) for 3 days at 31 to 40 C. in a 10-ml. beaker to which was added 0.2 ml. of toluene to inhibit growth of microorganisms. (A preliminary experiment had shown that the same amount of uronic acid-containing material was released in 2.6 days as in 10 days of treatment with trypsin.) The residue was removed by centrifugation at 25,000 × g for 40 to 60 minutes in a weighed centrifuge tube, washed 3 times with water and once with acetone, and weighed. In some instances 70 mg. of the residue from trypsin digestion was treated with 0.14 ml. of papain suspension† in 4.2 ml. of 0.1 M citrate buffer, pH 4.4, under the same conditions as the trypsin digestion but for 6 days. The residue was spun out at 25,000 × g for 15 minutes and washed in the same way as the trypsin residue. The supernatant and the water washes from a given digestion mixture were combined and made to 10-

* Operated by Union Carbide Corporation for the U. S. Atomic Energy Commission.

* The trypsin was a crystallized, lyophilized, salt-free preparation (TL 550) obtained from Worthington Biochemical Corporation.

† The papain was a crystalline suspension in 0.03 M cysteine (5450B) obtained from Worthington Biochemical Corporation.

ml. volume with water. Each sample was treated repeatedly with chloroform-amyl alcohol to remove protein (10) until only a slight emulsion formed at the interface. The resulting supernatant was then dialyzed a total of 40 hours at 0 to 5 C. against three 500-ml. portions of distilled water. By weighing the sample in the dialysis tubing before and after dialysis, a dialysis dilution factor was obtained. Duplicate 100-μl. samples for S^{35} measurement were taken before treatment with the chloroform-amyl alcohol reagent and before and after dialysis.

Hexuronic acid content of the purified supernatants from both trypsin and papain digests was estimated by the Dische procedure (2). In preparation for hexosamine analysis aliquots of the supernatants were hydrolyzed in 6 N HCl for 75 minutes at 100 to 110 C.; in our hands these conditions gave maximum liberation. For colorimetric estimation of hexosamine a variation* of Boas' modification (1) of the Elson-Morgan procedure was used. Analysis of 10 aliquots of a standard containing 25 μg. of glucosamine per aliquot gave a standard deviation of 3.7%. Since examination of the absorption spectra (between 500 and 600 mμ.) of the hydrolyzed trypsin and papain supernatants indicated only small amounts of interfering chromogens, no ion-exchange separation was carried out before analysis for hexosamines.

Some 5-mg. samples of whole powdered cartilage and 10-mg. samples of residues from trypsin digestion were analyzed directly for uronic acid content by the Dische procedure. In two cases 50 mg. of cartilage was treated directly with papain (0.1 ml. in 3 ml. of citrate buffer), and the reaction products were treated in the same way as the other enzyme digestion products.

* Two ml. of acetylacetone reagent and 2 ml. of Ehrlich's reagent (1.4% solution, weight per volume, of *p*-dimethylaminobenzaldehyde in 1:1 mixture of ethyl alcohol and concentrated hydrochloric acid) were used; final volume of each sample was 12 ml.

RESULTS

Two MPS fractions were found in rat costal cartilage. Fraction A, obtained by trypsin digestion of cartilage, contained S^{35} sulfate and equimolar amounts of uronic acid and hexosamine. This fraction decreased with age in relation to weight of dry cartilage (table 1, fig. 1). Two successive trypsin digestions of the same cartilage sample increased the amount of uronic acid-containing material released by trypsin only 2%. More than 90% of the radio-

TABLE 1. URONIC ACID AND HEXOSAMINE CONTENT OF MUCOPOLYSACCHARIDE FRACTION A OBTAINED FROM RAT COSTAL CARTILAGE BY TRYPSIN DIGESTION.

Age of Rat* (Days)	Content of Fraction A (μg./mg. of Dry Cartilage) after Indicated X-ray Doses									
	0 r		100 r		300 r		750 r		850 or 900 r	
	Ur. Acid	Hexosamine	Ur. Acid	Hexosamine	Ur. Acid	Hexosamine	Ur. Acid	Hexosamine	Ur. Acid	Hexosamine
56	33.2	30.2								
56	29.0	26.6								
102	25.0	27.7								
102	26.6	30.6								
114	22.2	—								
114	21.8	20.7								
239	15.7	15.8	14.2	15.0	14.2	15.2	13.8	14.7		
239	14.3	14.2	14.2	15.2	14.6	13.5	14.8	14.0		
249	18.6	17.7							15.6†	14.8†
251	16.3	15.4							15.0†	14.0†
339	17.7	17.4					15.8	15.2		
339	—	—					16.2	15.9		
436	14.5	13.5					10.1	9.8	13.6‡	13.8‡
436	13.1	11.9					11.8	11.8	10.4‡	10.3‡
436	13.2	15.6								
448	11.2	11.9								
448	11.4	11.3								
624	11.9	11.7								
624	9.5	9.2								
624	9.0	10.0								
624	9.3	9.8								
730	7.2	8.5								

* Each item, one rat (e.g., 56 days, 0 r)
† 900 r
‡ 850 r

active sulfur was found in the trypsin supernatant.

The MPS that remained in the residue from trypsin digestion and that was released into the supernatant by papain in citrate buffer, Fraction B, also contained equimolar quantities of uronic acid and hexosamine but was not sulfated. In addition, its concentration in cartilage changed very little with age, remaining about the same between 100 and 624 days of age (table 2, fig. 1).

Total uronic acid determined on whole powdered cartilage declined from 28 to 14 μg./mg. of cartilage between 100 days and 2 years of age.

Although the mean values of uronic acid and of hexosamine of Fraction A were lower in the 239- to 251-day-old and in the 436-day-old irradiated animals (750 to 900 r) than in controls of the same ages, the differences were not statistically significant by Student's *t* test (table 1). In Fraction B no differences in uronic acid and hexosamine content were apparent between irradiated and control animals 181 days after irradiation (table 2).

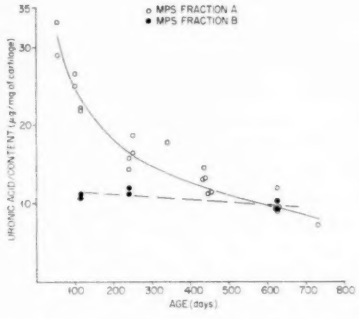

Fig. 1. Changes in uronic acid content of costal cartilage of rats with age. Open circles denote the amount of uronic in MPS Fraction A (see text); closed circles represent that in Fraction B.

Chromatography in pyridine-ethyl acetate-acetic acid-water (5:5:1:3) with pyridine-ethyl acetate-water (11:40:6) used to saturate the atmosphere (4) of hexosamines from hydrolyzates of whole cartilage [the method used was essentially that described by Stidworthy (12)] showed large amounts of galactosamine but only traces of gluocosamine.

Papain treatment only of dry cartilage released 87 to 100% of the S^{35} into the supernatant.

DISCUSSION

The decrease with age of our Fraction A of rat costal cartilage MPS followed the same general pattern as that of CSA in human costal cartilage reported by Stidworthy and associates (12), i.e., it declined rapidly during the maturation period and more slowly during the remainder of life. Kaplan and Meyer (7) reported linear decline of CSA in human costal cartilage. The rapid MPS change during the growth period of rats may be considered more properly to be a maturation change than a senescent change. The slower decline of Fraction A that occurred later in life apparently was not altered by subjection of the rats to whole-body X irradiation when they were about 2 months old, in contrast to various other senescent-type changes that are hastened by irradiation.

Our results indicate that the glucosamine-containing MPS, keratosulfate, that remains constant from young adulthood throughout life in man is absent from rat cartilage, or present only in very small amounts, since only trace amounts of glucosamine were found in hydroly-

TABLE 2. URONIC ACID AND HEXOSAMINE CONTENT OF MUCOPOLYSACCHARIDE FRACTION B OBTAINED BY DIGESTION WITH PAPAIN OF THE RESIDUE FROM TRYPSIN DIGESTION OF RAT COSTAL CARTILAGE.

Age of Rat* (Days)	Content of Fraction B (μg./mg. of Dry Cartilage) after Indicated X-ray Doses							
	0 r		100 r		300 r		750 r	
	Ur. Acid	Hexosamine	Ur. Acid	Hexosamine	Ur. Acid	Hexosamine	Ur. Acid	Hexosamine
114	10.7	—						
114	11.2	9.7						
239	12.0	10.6	11.1	8.8	11.8	10.7	11.1	10.6
239	11.2	9.8	11.9	8.2	11.5	9.0	11.5	10.4
624	9.8	8.8						
624	10.3	10.1						

* Each item, one rat.

zates of whole costal cartilage of 3.5- and 14-month-old rats. Our Fraction B, however, which contained equimolar amounts of uronic acid and hexosamine but no S^{35}, also remained relatively constant in amount in terms of μg. per milligram of cartilage from 115 to 624 days of age. This MPS constituted about 50% of the uronic acid-containing MPS in costal cartilage at older ages.

Failure of trypsin to release Fraction B into the supernatant indicates a different mode of linkage of this fraction to protein than of Fraction A. Lack of sulfate uptake by Fraction B indicates either an absence of sulfate in this fraction or a slow rate of sulfate turnover, since sulfate injected into the rats 24 hours before they were killed was highly concentrated in Fraction A.

SUMMARY

A sulfated mucopolysaccharide containing equimolar quantities of uronic acid and hexosamine was obtained from rat costal cartilage by digestion with trypsin. Its concentration decreased with age. A second MPS not released by trypsin also contained equimolar quantities of uronic acid and hexosamine but incorporated little or no sulfate in a 24-hour period. The concentration of the latter MPS in cartilage remained relatively constant between ages 115 and 624 days. Whole-body X irradiation of young rats did not affect the concentration of either MPS in later life.

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STUDIES ON HEXOSAMINE AND COLLAGEN IN TISSUES OF RATS WHICH SURVIVED X-IRRADIATION*

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It is generally agreed that life span is shortened in animals which have survived radiation injury (1, 13). Indeed shortening of life span has been reported following doses insufficient to produce early mortality. The causes of life-shortening relate to the induction of neoplasia with increased frequency, often of unusual distribution, and to the premature appearance of a variety of conditions commonly designated as degenerative. Certain clinical and histologic observations lead to the concept that radiation has accelerated natural aging processes. However, it seems that the final acceptance of such a concept must await the detection of quantifiable biochemical or physiological phenomena which are time-associated and which occur independently (initially at least) of any histopathological events, and finally the demonstration that these age-associated phenomena are accelerated following irradiation.

The hexosamine-collagen ratio (H/C) of connective tissues has been proposed as a measure of biochemical age (8, 11). This derives from the fact that collagen accumulates in connective tissue because of its relative metabolic inertia (3, 9). The constituents of the ground substance, including the mucopolysaccharides (as measured by hexosamine), remain in dynamic equilibrium with the remainder of the organism. H/C then is to be taken as an inverse measure of fibrillar density and it decreases with age (11). It has been suggested that the decrease in H/C would result in interference with the rate of delivery of oxygen and nutrients to the cells and rate of delivery of waste products from the cells (6). Since the variables involving the chemical and physical state of the ground substance are numerous, this proposal must be an extreme oversimplification. Nevertheless, it serves as a useful working hypothesis.

If irradiation accelerates aging, animals thus exposed should show lower H/C values in connective-tissue-rich organs than those of similar age which were not exposed. A study was therefore undertaken of the H/C of the skin, femur, sternum, lung, aorta, and vena cava of post-irradiated rats. It was observed that survivors of a dosage sufficient to cause early mortality in excess of 30% exhibited evidence of premature aging according to these criteria.

METHODS

Wistar rats were obtained from a commercial source. The males weighed approximately 175 Gm. and the females approximately 150 Gm. They were maintained on Purina Chow until the completion of the experiment and were irradiated after 1 to 2 weeks in the laboratory. The irradiation groups consisted of 36 animals each, while 18 or 24 were maintained as controls for each group.

Irradiation was carried out with facilities available at the University of Southern California: A) General Electric Maximar, 250 - III, 200/260 volt apparatus; B) Radiation chamber with a wooden box having a plastic top made of cellulose acetate 1/8"; the intensity of the irradiation was standardized by measurement with the Victoreem (r) meter; C) Box divided into compartments, so made that animal could be placed comfortably; the irradiation chamber was constantly rotating on a rotating table; to prevent overheating, a fan was placed at the same level of the wooden box (2).

The survivors were killed after 15-18 months. In the case of groups I ♂ and I ♀ the complete skin (except for that over the legs and head) and a complete femur were taken. In the other cases small pieces of tissues were obtained in a uniform manner sufficient to make triplicate analysis.

The procedure for analyzing specimens rich in connective tissue for collagen (C) and hexosamine (H) has been described (7, 11). The tissues were analyzed directly for these con-

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stituents without weighing. It was assumed that all of the hydroxyproline was present in collagen. Obviously in the case of the lung, aorta, and vena cava it is not correct to refer to fibrillar density without analysis for elastin. Nevertheless the application of this term to H/C data on these tissues has been found to be useful (7). Because this project was carried out over a period of 3½ years, during which time changes in personnel and minor changes in technique had taken place, the values of the analytical data are not strictly comparable between groups.

RESULTS

Following a dose of 520 r, statistically significant differences in H/C were observed in the lung but not in skin, femur, aorta, and vena cava of survivors (the sternum was not studied in group I♂) (table 1). In the case of the lung the mean H/C value was approximately −8% of that of the unirradiated rats. Following 540 r, significantly lower values were observed in sternum (−14%) but not in other organs. The values for the lung were only slightly below those of the controls. Since the mean femur length for the irradiated group was somewhat lower than that of the control animals, somewhat larger H/C values would be expected if the former were normal (12). Thus the effect upon lung observed following 520 r may be masked by comparison with the larger controls. Following a larger dose (560 r) survivors had significantly lower H/C values in skin (−14%), sternum (−75%), lung (−11%), and aorta (−13%) than their controls. Similar observations were made in a group of female rats which had received 540 r (exclusive of the sternum, which was not investigated in group I♀). Significantly lower H/C values were observed in femur (−9%), lung (−4%), aorta (−9%), and vena cava (−4%). Although the value for the skin was considerably less than that of the controls (−18%), the difference was not statistically significant. Eight irradiated animals had large mammary tumors, and their tissues were analyzed as a separate group. The H/C values were again lower for femur (−10%), lung (−5%), aorta (−15%), and vena cava (−7%. Interestingly enough the H/C value for skin was similar to that of the controls. The only explanation which comes to mind relates to the increased quantity of circulating mucopolysaccharides which occurs in tumor-bearing

TABLE 1. H/C VALUES IN SKIN, FEMUR, STERNUM, LUNG, AORTA, AND VENA CAVA OF RATS SURVIVING RADIATION INJURY.

Group		Dosage of X-ray	Mortality 30 Days	† Mortality at Term	‡ No.	Wt. (Gm.)	Femur Length (cm.)	Skin	Femur	Sternum	Lung	Aorta	Vena Cava
I♂	I	520r	2/36	10/36	14	468	3.83§	.0061	.0202	.....	.0517*	.170	.113
								±.0001‖	±.0003	.....	±.0003	±.002	±.001
	C	.....	0/24	6/24	16	462	3.83	.0063	.0209	.....	.0560	.165	.111
								±.0001	±.0003	.....	±.0005	±.001	±.001
II♂	I	540r	5/36	15/36	18	430	3.64	.0065	.0290	.0430*	.0560	.065	.045
								±.0002	±.0011	±.0011	±.0005	±.001	±.001
	C	.....	1/18	6/18	12	457	3.81	.0062	.0281	.0490	.0570	.065	.045
								±.0001	±.0004	±.0012	±.0007	±.001	±.001
III♂	I	560r	(18/36)**	24/36	12	479	3.86	.0067*	.....	.0193*	.0560*	.054*	.039
								±.0003	.....	±.0010	±.0009	±.001	±.002
	C	.....	0/18	5/18	12	564	3.92	.0078	.....	.0440	.0652	.061	.040
								±.0002	.....	±.0011	±.0010	±.001	±.002
I♀	I	540r	12/36	19/36	8	296	3.46	.0057	.0225*	.....	.0496*	.125*	.096*
								±.0004	±.0002	.....	±.0001	±.001	±.001
	I_T	.....	.....	.....	8	287	3.44	.0066	.0224*	.....	.0494*	.117*	.092*
								±.0007	±.0003	.....	±.0004	±.001	±.001
	C	.....	0/24	7/24	10	316	3.45	.0067	.0246	.....	.0518	.135	.100
								±.0004	±.0003	.....	±.0004	±.001	±.001

I = irradiated; I_T = irradiated with mammary tumors; C = controls.

* P value < .05.

† Total mortality at time of sacrifice.

‡ Number of animals from which specimens were taken for analysis. This does not necessarily include all the survivors.

§ Mean femur length is shown because this is a function of maximum growth. Since body weight will be affected by differences in fat and water content, femur length has been used in this laboratory as a means of determining body size for comparing quantifiable data obtained from organ analysis.

‖ Standard error.

** Approximations—actual value uncertain

organisms (15) and that perhaps some of these materials are deposited in the skin.

From the foregoing it does seem that the H/C values of connective tissue-rich organs of animals in which high early mortality is induced by single doses of X-ray are lower than the H/C values of unirradiated animals. It seems that a mortality in excess of 30% must be induced before these differences become generally apparent.

In order to determine whether the decrease in H/C is due to a decrease in hexosamine-containing material or an increase in collagen, it is necessary to compare contents of complete organs (12). This was possible in the case of the skin and femur of groups I ♂ and I ♀ (table 2). The hexosamine contents of the femurs in the irradiated rats were identical with their controls. In the case of the skin the hexosamine contents for groups I ♂ and I ♀ were 4% and 10% less than their controls, but these differences were not statistically significant. The collagen contents of the femurs was greater than that of the controls (6 - 8%), and these differences were statistically significant. The skin from the I ♀ group contained in excess of 9% more collagen than the unirradiated controls but this difference was not statistically significant.

DISCUSSION

In order to prove that any external factor may cause acceleration of natural aging processes, it is necessary to establish the following criteria: 1) The existence of seemingly irreversible quantifiable biochemical or physiological phenomena which progress with time independently of pathological events (however, the progression of these phenomena may cause or increase susceptibility to pathological events); 2) That following exposure to the external influence, values are obtained for the quantifiable phenomena which in the absence of exposure would not occur until additional time had elapsed.

Although life span is shortened by irradiation and certain clinical and histopathological events occur prematurely, proof that this can be considered to represent acceleration of natural processes is yet to be obtained.* This can come about only when the above criteria are fulfilled.

The determination of H/C in connective-tissue-rich organs represents an attempt to find a quantifiable device as indicated above. The decrease in H/C represents an increase in fibrillar density and its application to the measurement of aging seems to be justified from a study on patients (11) and from a description of certain histological events which occur with aging (14). Employing this as a criterion, the data presented above indicate that following a dose of X-ray sufficient to cause early phase mortality in excess of 30%, tissues rich in connective components have lower H/C values than their unirradiated controls. This is consistent with the concept that accelerated aging has occurred. It should be pointed out that the conclusions are based on the ratio of H to C and not on absolute values, since the tissues were not weighed.

If the H/C ratio relates to the fibrillar density, a decrease in H/C could be effected by withdrawal of ground substance (and with it hexosamine-containing mucopolysaccharides) or by accrual of collagen. It has been shown that loss of hexosamine occurs in nitrogen wastage as a result of starvation or cortisone administration (7). In the post-irradiated animal, if premature aging occurred it would be expected that

* Too often aging phenomena, the pathology of the aged organism, and the causes of death are considered to be equivalent. Aging phenomena are a consequence of normal vital phenomena and are an inevitable result of these normal vital phenomena. In this sense they are not pathological. The progression of the phenomena may increase susceptibility to pathological processes, however. The author (H.S.) believes that the failure to make this distinction is hampering progress in this area.

TABLE 2. HEXOSAMINE (H) AND COLLAGEN (C) CONTENT† OF SKIN AND FEMURS OF RATS SURVIVING RADIATION INJURY.

Group		Skin		Femur	
		H (mg.)	C (mg.)	H (mg.)	C (mg.)
1♂	I	30.0±2.7	4915±313	2.07±.05	100.6±2.9*
	C	31.2±1.5	4996±301	2.07±.05	93.5±1.6
1♀	I	14.4±1.3	2541±153	1.52±.04	67.0±1.7
	I_T‡	.....	.....	1.54±.02	68.3±1.0*
	C	15.9±1.2	2322±85	1.56±.03	63.4±.9

* P value < .05.

† These values do not represent hexosamine and collagen per unit weight of tissue (since the tissues were not weighed) but pertain to the total quantity present.

‡ The complete skin could not be obtained because the animals carried large mammary tumors which eroded through the organ.

the appearance of the aging syndrome (10) would be accompanied by a loss of body nitrogen. Furthermore if age-associated changes in steroid production which occur in the human (4, 10) occur likewise in the rat, it would be expected that the metabolic effects similar to that induced by cortisone administration would become manifest (7). Since radiation injury could accelerate this change (as does chronic illness, 10), the antianabolic influence of the corticoids should soon become manifest. In this way the effect of radiation could be that of a non-specific injury. Aging has been interpreted as an accumulation of the effect of non-specific injuries sustained throughout life (5).

From the foregoing it was expected that if evidence of premature aging occurred (as manifested by decrease in H/C) it would be associated with a decrease in the hexosamine-containing component. This did not seem to be the important factor, however, since the hexosamine contents of the skin and femur of groups I♂ and I♀ were not significantly less than that of their age controls. However, the collagen content of the femurs was greater in the irradiated group. Although these data are meager, they suggest a semi-specific modality by which radiation injury may accelerate aging (in addition to its role in non-specific injury and as a mutagen). The reasoning behind this hypothesis is as follows: It is well known that fibrillogenesis occurs following a variety of factors which cause death of parenchymal cells. These include trauma, infection, hypoxia, and other necrogenic agents. This phenomenon has not yet been adequately explained. Is it possible that an environment which is lethal to parenchymal cells may under certain circumstances be optimal for mesenchymal cells and that fibrillogenesis is restrained under conditions which are optimal for parenchymal cells? If this is the case the acceleration of aging following radiation injury might be due to the following scheme: After irradiation large masses of cells die or have their functions greatly impaired. Before adequate repair is possible, the fibroblasts find an environment optimal for vigorous collagen production and fibrillogenesis, the greater the radiation damage, the more vigorous the fibroblastic activity. Thus organs which have suffered the greatest damage would show the greatest increase in collagen content. This seems to be an exciting area for further investigation.

SUMMARY

The ratio of hexosamine to collagen was determined in skin, femur, sternum, lung, aorta, and vena cava of rats which had survived X-ray treatment administered in one dose from 15 - 18 months previously. It was observed that the ratios were lower than that of unirradiated animals of similar age if early phase mortality had exceeded 30%. This seemed to be due to a significant increase in collagen content. The hexosamine content seemed to be reduced but not significantly. These findings are consistent with the concept of accelerated aging in animals which survive irradiation damage. It is suggested that in part this phenomenon is due to increased fibrillogenesis following death or injury of parenchymal cells.

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THE DEPOSITION OF AGING PIGMENT IN THE HUMAN CEREBRAL CORTEX

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A frequently described concomitant of aging is the development and accumulation of a pigmented material within the cytoplasm of nerve cells. This pigment has been described in neurons of the cerebellum (7, 8), autonomic ganglia (6, 10, 16, 17, 19), spinal ganglia (2, 5) and the spinal cord (3, 4).

Gardner (5) considered the presence of pigment in spinal ganglion cells to be related to age. Sulkin and Kuntz (19) found the sympathetic ganglion cells to contain pigment granules in children and adults up to 90 years of age. They were unable to demonstrate a progressive increase in pigment concentration in human sympathetic ganglia cells with age. However, the presence of this material was frequently observed in dogs after 12 years of age, although not present in a series of dogs aged 30 days to 9 years. On this basis, these authors considered pigmentation to be definitely associated with aging in this animal. Although usually related to the adult organism, pigment may occasionally be found in multipolar neurons of the spinal cord of the human fetus (9).

Although pigment has been observed in cells of the cerebral cortex of man (1, 12, 15, 21), no attempt has been made to determine quantitatively the relationship between pigment and aging in these cells. The purpose of this study was to investigate the differences in pigment deposition in several areas of the cerebral cortex and to establish whether a relationship exists between pigment and aging in cortical cells.

MATERIAL AND METHODS

This study is based upon examinations of 20 brains from individuals ranging in age from newborn to 95 years. These specimens were removed from individuals who had died of causes which would not ordinarily be expected to have affected the nerve cells of the cortex. After two days of initial fixation in 10% formalin, blocks were cut and placed into 10% formol-saline. Blocks of tissue were removed from the precentral and postcentral gyri, the superior temporal gyrus, and the striate area.

After dioxan dehydration, the blocks were infiltrated and embedded in paraffin and sections cut at 10μ. Sections were stained by the Purves and Griesbach modification (14) of the McManus periodic acid-Schiff technique (11).

Preliminary observation revealed that when pigment was found in the cortex, the greatest amount was located in the cells of the pyramidal layer (layer III). This layer was therefore chosen for the study. One hundred nerve cells through this layer were examined in series for concentration of pigment. The cells were divided into three groups as follows: Group 1, cells lacking pigment; Group 2, cells containing pigment scattered throughout the cytoplasm (fig. 1); Group 3, cells showing an aggregation of pigment granules (fig. 2). The specimens in this study were separated into 4 age classes: newborn to two months, 16 to 21 years, 45 to 48 years, and 70 to 95 years. Five individuals were included in each class. The percentages of cells in each group was then transposed to graphs (fig. 3) to permit comparison of the pigment distribution in these cortical areas with increasing age. These percentages were calculated after the examination of 1000 cells within layer III in each cortical area. As a further check, these cells were counted upon 3 different occasions.

RESULTS AND DISCUSSION

It may be noted (fig. 3) that in the youngest age period there is no pigment deposition in the cells of the third cortical layer. Examination of other layers of the cerebral cortex also failed to reveal the presence of lipofuscin material in these specimens. Although Humphrey (9) had noted occasional cells with pigment in the spinal cord of the human fetus, neither Pilcz (13) nor Obersteiner (12) found pigment in central nervous system tissue in the newborn. They noted that pigment appeared in the cells

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of posterior root ganglia at 6 years of age and in the spinal cord at 8 years. The findings in the spinal cord by these investigators have been confirmed by Chu (3), who studied anterior horn cells isolated from human lumbar spinal cord.

As one proceeds through the adult age groups, there is a sharp decrease in the number of cells free of pigment and an increase in the number of cells containing pigment. In the older age groups the majority of cortical cells contain pigment. However, the greater number of these pigmented cells contain scattered pigment and only a relatively small number showed clumped pigment in the cytoplasm. Therefore, while the number of cells containing pigment increases with increasing age, the actual number of cells which show a great accumulation of pigment is relatively low.

While Chu (3) found that in the human spinal cord the amount of pigment increases with age of the individual, and Wilcox (20), after examination of the cranial nerve nuclei in the guinea pig, stated that the accumulation of lipofuscin is the only alteration that occurs constantly enough to be correlated with aging, the major finding in the human cerebral cortex is that the greatest correlate with age is the number of cells containing scattered pigment and not necessarily those filled with great amounts of pigment. A necessary prerequisite for a study of pigmentation is a staining technique which sharply differentiates lipofuscin from other cytoplasmic structures (18). This is not possible with a thionin (3, 20) or cresyl violet preparation in which the pigment may be obscured by stained structures other than pigment granules. This danger is obviated by the use of the PAS technique, which reveals the presence of scattered granules that might easily be overlooked with the usual central nervous system stains.

Examination of figure 3 reveals that the highest percentage of heavily pigmented (Group 3) cells was found in the precentral gyrus, while the lowest percentage of this type was in the striate cortex. The observations in the precentral gyrus coincide with cellular size, with a

Fig. 1. Photomicrograph of a Group 2 cell from layer III of the precentral gyrus of human cerebral cortex indicating pigment granules scattered in the cytoplasm. PAS preparation with hematoxylin counterstain. X 1,000.

Fig. 2. Photomicrograph of a Group 3 cell from layer III of the precentral gyrus of human cerebral cortex indicating congregation of pigment granules in the cytoplasm. PAS preparation with hematoxylin counterstain. X 1,000.

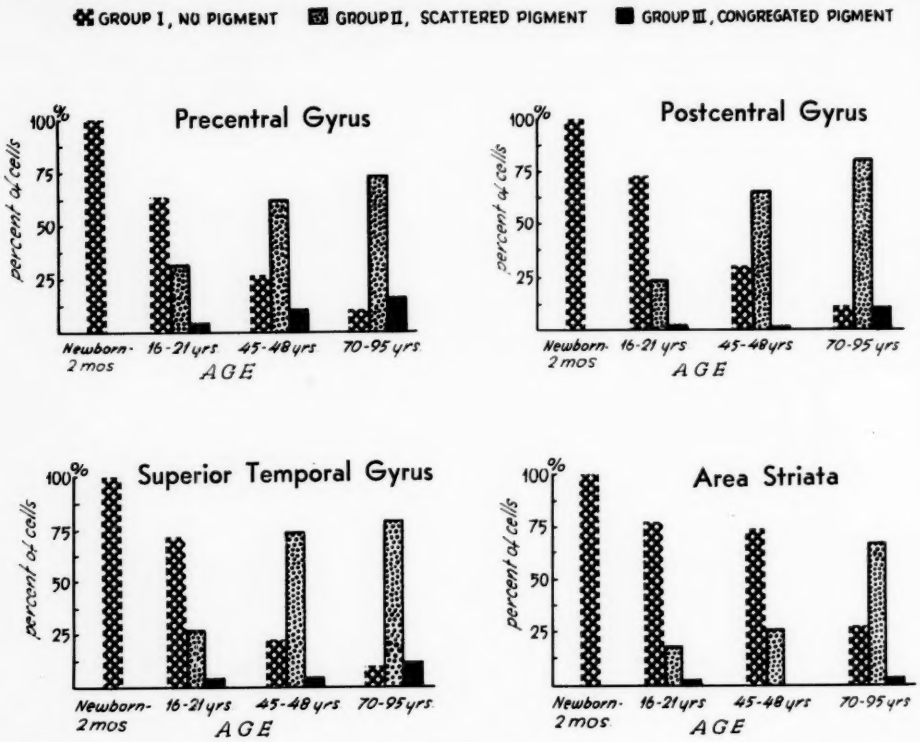

Fig. 3. The relationship according to age of the distribution of pigment within cells of layer III in the human cerebral cortex.

direct relationship between cell size and aggregation of pigment material. One would, therefore, expect that in areas where cortical cells are generally smaller in size, the number of cells showing great accumulations of pigment is extremely low. This is true of the striate cortex where histologically the tissue is composed of extremely small-sized cells. Consequently, there is a basis for the higher number of cells in this area containing little or no pigment. Also to be noted is the very slight decrease in Group 1 cells in the striate cortex between the young adult and middle-aged periods. This is in contrast with other areas examined in which there is a generally sharper decrease in these cells during these two age periods. The decrease in the Group 2 cells in striate cortex between 45-48 years and 70-95 years is more in relation with that occurring in other cortices at younger ages. The higher percentage of Group 3 cells in the precentral gyrus is due in part to the number of larger-sized pyramidal cells within the third layer. Observation of the Betz cells within layer V of the precentral gyrus also indicates a large number of cells which would fit into the Group 3 classification. This relationship between large cell size and heavy pigment deposition may also be seen in the anterior cell column of the spinal cord and in motor cranial nerve nuclei. However, it should be noted that in the cerebral cortex the number of these large sized cells is small and, although one may be overly impressed with the occasional cell with much pigment, the majority of cells fit into the category of the Group 2 type cell which can be recognized only after the use of a differential stain.

SUMMARY AND CONCLUSIONS

A semiquantitative study was made of lipofuscin deposition in the cells of the third layer of the cerebral cortex of the precentral gyrus, post-central gyrus, superior temporal gyrus, and the striate cortex in order to determine its relation to age.

Examination of 20 human brains between the ages of newborn and 95 years shows that a relatively small number of cells in the aged group contained what might be considered to be excessive amounts of pigment. The majority of cells contained smaller amounts of pigment scattered throughout the cytoplasm.

The cells of the newborn are free of lipofuscin pigment. With progressing age there is an increase in the percentage of cells containing small amounts of pigment with a corresponding decrease in the percentage of pigment-free cells.

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THE ISOCITRIC DEHYDROGENASE AND TPN-MALIC ENZYME ACTIVITIES OF ARTERIAL TISSUE IN INDIVIDUALS OF VARIOUS AGES*

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Both of the enzymes, isocitric dehydrogenase and TPN-malic enzyme included in the present study, possess the feature of being TPN-dependent. Since it has been shown in recent years (3, 4, 8) that TPNH is a requirement for the synthesis of cholesterol and fatty acids, a study of the activities of these two enzymes in human arterial tissue would seem to be of special interest. The presence in the arterial tissue of two other TPN-dependent enzymes, glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase, has been reported in a previous publication from this laboratory (2).

MATERIALS AND METHODS

Seventy samples of the aorta (thoracic descending), 60 samples of the pulmonary artery, and 43 samples of the coronary artery were included in the study. The arterial samples were obtained fresh at autopsy at the St. Louis City Morgue from subjects ranging in age from 0 to 85 years. After removal of the adventitia the tissue was rinsed briefly with ice-cold isotonic sodium chloride solution in order to eliminate contamination from adhering blood; for the same reason, only tissue portions which on examination were found to contain no blood capillaries were employed for the studies. In the case of the aortic and coronary artery samples, the activity measurements were made both on normal and arteriosclerotic tissue sections of the same blood vessels. Five per cent homogenates were prepared of the intima-media layers of the arterial samples by homogenization of the tissue for 2 minutes in ice-cold isotonic sodium chloride solution with the use of a Pyrex homogenizer. The homogenates were subsequently centrifuged for 10 minutes at 4000 r.p.m., and the supernatants were employed for the activity assays. The activity measurements were carried out by modifications of Ochoa's procedures (6, 7) through determination of the rate of reduction of TPN at 38 C., using, respectively, D-L-isocitrate and L-malate as substrates. A Beckman DU spectrophotometer provided with thermospacer equipment was employed for the enzyme tests.

The completeness of extraction of the enzymes from the arterial tissue by the procedure described above was ascertained in special experiments in which the precipitate obtained after centrifugation of the prepared homogenate was rehomogenized with a new portion of sodium chloride solution. After centrifugation of the second homogenate, the isocitric dehydrogenase and TPN-malic enzyme activities of the resultant supernatant were measured. It was found that the second supernatant showed only low enzyme activities and that these activities corresponded closely to the values estimated on the basis of the volume and water content of the first residue.

The enzyme activities listed in the present publication, which are expressed both on the basis of wet tissue weight and tissue nitrogen content, refer to the weight and nitrogen content of the original tissue samples from which the supernatants were prepared.

Isocitric dehydrogenase.—The final millimolar concentrations used (total volume, 3.05 ml.) were: D-L-isocitrate, 3.3; TPN, 0.35; manganese sulfate, 1.64; Tris, 33.0; the pH of the substrate-buffer mixture was 7.5. After preheating of the substrate-buffer mixture for 3 minutes at 38 C. in a silica cuvette, the reaction was started by addition of 250 cu. mm. of the supernatant, corresponding to 12.5 mg. of tissue, to the sample. After rapid mixing of the contents of the cuvette, readings of the optical density were made at 340 millimicrons at regular intervals over a 15 to 20-minute period. In the case of measurements performed on supernatants prepared from arteriosclerotic tissue samples, the cuvette content was stirred with a plastic stirrer 20 seconds before each reading. A reagent blank, a tissue control without isocitrate, and a control without TPN were run with each tissue test. The reaction curve for the tissue test was found to be linear with time under the experimental conditions used over a period of at least 15 minutes, and a close relationship was observed between the quantities of tissue used and the recorded enzyme activities for a 5 to 25 mg. tissue range.

The observed K_m calculated for D-isocitrate was 1.53×10^{-4} M. The optimal pH for the isocitric dehydrogenase activity was found to be 7.5, but a change of the reaction to 7.0 or 8.0 resulted in less than 20% decrease in activity (fig. 1). Experiments were further conducted to investigate the relation between the manganese sulfate concentration used and the enzyme activity. As seen from figure 2, the results showed essentially similar activities over a concentration range from 0.66 to 3.28 mM. The activity in the absence of manganese sulfate was only about 10% of that observed in the presence of the optimal manganese concentration.

TPN-malic enzyme.—In the TPN-malic enzyme activity determinations, similar final concentrations of TPN, manganese sulfate, and Tris buffer were employed as in the isocitric dehydrogenase assays. The L-malate concentration used was 3.9 mM, and the pH of the substrate-buffer mixture was 7.9. The activity measurements were carried out in a manner similar to that described for isocitric dehydrogenase, and for the TPN-malic enzyme the rate of TPN reduction was also found to be proportional with time over a 15-minute period and for a 5 to 25 mg. tissue range.

Studies on Arterial Metabolism 31. The investigation was supported by a grant from the National Institutes of Health, Public Health Service (PHS-891). A report of this study was presented at the 50th Annual Meeting of the American Society of Biological Chemists, Atlantic City, N. J., April 14, 1959 (*Fed. Proc., 18:* 261, 1959).

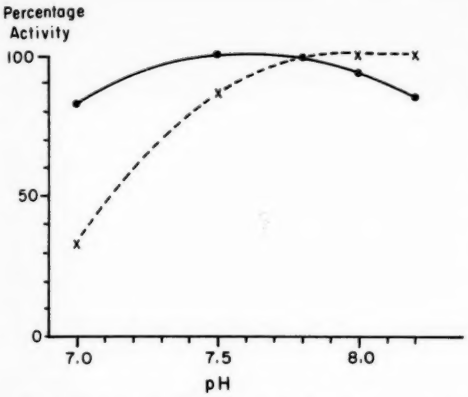

Fig. 1. Effect of pH on isocitric dehydrogenase and TPN-malic enzyme activities of aortic tissue sample.
——————— Isocitric dehydrogenase
- - - - - - - - - - - - - TPN-malic enzyme

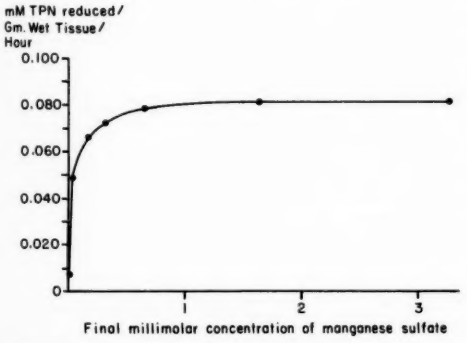

Fig. 2. Effect of manganese sulfate concentration on isocitric dehydrogenase activity of aortic tissue sample.

The observed K_m for L-malate was 3.18×10^{-4} M. In accordance with the observations by Van Heyningen and Pirie (9) the optimal activity was recorded at a pH range from 7.8 to 8.2. A change in pH toward the acid side beyond this range was followed by a considerable decrease in the activity of the enzyme (fig. 1). Thus the activity observed at pH 7.0 was only 35% of that recorded at pH 7.9, the pH used in the standard procedure.

Practically identical activity values were found at final manganese sulfate concentrations of 1.64, 3.28, and 4.26 mM, whereas a 25% decrease occurred when the concentration was reduced to 0.33 mM.

RESULTS

The mean isocitric dehydrogenase and TPN-malic enzyme activities of aortic, pulmonary artery, and coronary artery samples observed for various age groups have been listed in table 1.

Isocitric dehydrogenase.—The average isocitric dehydrogenase activities found for normal aortic, pulmonary artery, and normal coronary artery tissue samples were, respectively, 0.064, 0.071, and 0.084 millimoles of TPN reduced/ Gm. wet tissue/ hour. The corresponding mean values, expressed on the basis of the tissue nitrogen content, were 1.71, 2.01, and 2.53. As seen from table 2, no significant correlations between age and enzyme activities were observed for the three types of arteries. In the case of both the aorta and coronary artery, essentially similar mean activity values were found for the arteriosclerotic and normal tissue portions of the same blood vessels (table 3).

TPN-malic enzyme.—The TPN-malic enzyme activity of the human arterial tissue was on the whole found to be only 15 to 20% of the isocitric dehydrogenase activity of the tissue. Thus the mean TPN-malic enzyme activities observed for the normal aortic, pulmonary artery, and normal coronary artery samples were, respectively, 0.0127, 0.0107, and 0.0124 millimoles of TPN reduced/Gm. wet tissue/hour, and the corresponding values, expressed on the basis of tissue nitrogen content, were 0.33, 0.31, and 0.38. In accordance with the findings for the isocitric dehydrogenase, no statistically important variation in enzyme activity with age was found (table 2). Similarly, a comparison of the mean enzyme activities of arteriosclerotic and normal tissue portions showed no significant differences between the values (table 3).

DISCUSSION

The present study has demonstrated the presence of isocitric dehydrogenase and TPN-malic enzyme in human arterial tissue. A comparison of the activities of these enzymes with the values previously observed for two other TPN-dependent enzymes of the tissue, glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase (2), shows that the isocitric dehydrogenase activity of the arterial tissue is slightly lower than that of glucose-6-phosphate dehydrogenase and that the activities of TPN-malic enzyme and 6-phosphogluconate dehydrogenase are of the same order of magnitude.

Determinations of the isocitric dehydrogenase activity of human serum and red blood cells have been reported by Wolfson and Williams-Ashman (10). On the basis of the data provided by these authors it can be calculated that the isocitric dehydrogenase activity observed per

TABLE 1. MEAN ISOCITRIC DEHYDROGENASE AND TPN-MALIC ENZYME ACTIVITIES OF HUMAN ARTERIAL TISSUE IN VARIOUS AGE GROUPS

			Isocitric Dehydrogenase				TPN- Malic Enzyme			
Age Group (Years)	N	Cholesterol, % of Wet Weight	mM TPN Reduced/ Gm. Wet Tissue/ Hour	s. d. of distr.	mM TPN Reduced/ Gm. Tissue N/ Hour	s. d. of distr.	mM TPN Reduced/ Gm. Wet Tissue/ Hour	s. d. of distr.	mM TPN Reduced/ Gm. Tissue N/ Hour	s. d. of distr.
Normal Aortic Tissue										
0– 9	13	0.1	0.064	0.031	1.59	0.84	0.0123	0.0093	0.30	0.25
10–19	2	0.3	0.064	.....	1.61	....	0.0138	.....	0.36	....
20–29	4	0.3	0.066	.....	1.67	....	0.0142	.....	0.37	....
30–39	7	0.4	0.057	0.016	1.44	0.34	0.0121	0.0032	0.30	0.10
40–49	12	0.4	0.065	0.014	1.70	0.36	0.0123	0.0050	0.32	0.12
50–59	16	0.5	0.067	0.013	1.86	0.38	0.0139	0.0031	0.38	0.09
60–69	13	0.8	0.066	0.013	1.84	0.23	0.0128	0.0038	0.35	0.11
70–79	2	0.6	0.052	.....	1.44	....	0.0100	.....	0.28	....
80–85	1	0.6	0.041	.....	1.30	....	0.0088	.....	0.28	....
Grand Mean..	..	...	0.064	0.018	1.70	0.48	0.0127	0.0055	0.33	0.15
Arteriosclerotic Aortic Tissue										
10–19	1	0.8	0.077	.....	1.78	....	0.0068	.....	0.16	....
20–29	2	0.5	0.055	.....	1.54	....	0.0105	.....	0.30	....
30–39	7	0.5	0.051	0.017	1.23	0.62	0.0096	0.0034	0.22	0.08
40–49	10	1.0	0.066	0.015	1.82	0.48	0.0129	0.0054	0.34	0.14
50–59	14	1.2	0.060	0.013	1.79	0.30	0.0120	0.0041	0.35	0.11
60–69	11	1.7	0.063	0.022	1.92	0.42	0.0114	0.0035	0.35	0.12
70–79	2	1.0	0.057	.....	1.65	....	0.0090	.....	0.26	....
80–85	1	1.0	0.059	.....	1.47	....	0.0071	.....	0.21	....
Grand Mean..	..	...	0.060	0.017	1.74	.046	0.0113	0.0043	0.32	0.12
Pulmonary Artery Tissue										
0– 9	9	0.2	0.061	0.024	1.53	0.56	0.0113	0.0082	0.24	0.18
10–19	2	0.3	0.053	.....	1.41	....	0.0126	.....	0.34	....
20–29	2	0.2	0.082	.....	2.14	....	0.0091	.....	0.23	....
30–39	6	0.2	0.070	0.026	1.92	0.82	0.0096	0.0043	0.26	0.16
40–49	11	0.3	0.078	0.047	2.29	1.50	0.0111	0.0038	0.31	0.13
50–59	14	0.3	0.073	0.032	2.11	0.96	0.0130	0.0037	0.37	0.08
60–69	13	0.3	0.073	0.017	2.19	0.58	0.0095	0.0041	0.27	0.12
70–79	2	0.3	0.068	.....	2.02	....	0.0097	.....	0.31	....
80–85	1	0.4	0.039	.....	1.24	....	0.0051	.....	0.16	....
Grand Mean..	..	...	0.071	0.028	2.01	0.88	0.0107	0.0049	0.31	0.14
Normal Coronary Artery Tissue										
0– 9	3	0.2	0.079	.....	2.48	....	0.0092	.....	0.26	....
10–19	1	0.3	0.121	.....	3.22	....	0.0270	.....	0.73	....
20–29	3	0.3	0.081	.....	2.38	....	0.0143	.....	0.42	....
30–39	5	0.2	0.091	0.033	2.77	0.95	0.0110	0.0070	0.34	0.21
40–49	7	0.3	0.100	0.018	2.66	0.46	0.0116	0.0067	0.27	0.13
50–59	11	0.6	0.069	0.018	2.08	0.68	0.0113	0.0058	0.36	0.26
60–69	10	0.4	0.085	0.023	2.78	0.90	0.0137	0.0048	0.51	0.17
70–79	2	0.2	0.081	.....	2.70	....	0.0133	.....	0.45	....
80–85	1	0.1	0.063	.....	1.84	....	0.0093	.....	0.27	....
Grand Mean..	..	...	0.084	0.023	2.53	0.73	0.0124	0.0059	0.38	0.18
Arteriosclerotic Coronary Artery Tissue										
30–39	3	0.8	0.092	.....	1.33	....	0.0122	.....	0.25	....
40–49	4	2.1	0.108	.....	3.96	....	0.0148	.....	0.53	....
50–59	8	1.7	0.082	0.035	2.63	1.30	0.0118	0.0051	0.37	0.17
60–69	8	2.0	0.080	0.029	2.60	1.03	0.0115	0.0039	0.39	0.14
70–79	2	1.2	0.082	.....	1.53	....	0.0088	.....	0.17	....
80–85	1	1.9	0.082	.....	2.10	....	0.0133	.....	0.34	....
Grand Mean..	..	...	0.086	0.029	2.66	1.03	0.0121	0.0045	0.39	0.18

TABLE 2. COEFFICIENTS OF CORRELATION BETWEEN AGE AND ARTERIAL ENZYME ACTIVITIES

	Wet Tissue		Tissue Nitrogen	
	r	t	r	t
Isocitric Dehydrogenase				
Aorta	−0.05	0.40	+0.12	0.96
Pulmonary Artery	+0.09	0.68	+0.20	1.50
Coronary Artery	−0.14	0.88	−0.19	0.96
TPN- Malic Enzyme				
Aorta	0.00	0.00	+0.10	0.75
Pulmonary Artery	−0.10	0.70	+0.11	0.72
Coronary Artery	−0.04	0.25	−0.07	0.32

TABLE 3. MEAN ENZYME ACTIVITIES OF ARTERIOSCLEROTIC TISSUE EXPRESSED IN PERCENTAGE OF ACTIVITIES OF NORMAL TISSUE OF THE SAME ARTERIAL SAMPLES

Age Group (Years)	N	Isocitric Dehydrogenase				TPN- Malic Enzyme			
		Wet Tissue		Tissue N		Wet Tissue		Tissue N	
		%	t of diff.	%	t of diff.	%	t of diff.	%	t of diff.
Aortic Samples									
30-49	17	100	0.00	99	0.18	97	0.48	98	0.26
50-59	14	91	1.67	98	0.38	88	1.15	92	1.13
60-85	14	100	0.00	106	0.84	95	0.61	100	0.00
30-85	45	97	0.93	101	0.32	94	1.36	97	1.09
Coronary Artery Samples									
30-85	26	104	0.62	103	0.57	97	0.52	97	0.52

gram of arterial tissue is about 300 times higher than that exhibited by 1 ml. of serum and approximately 4 times higher than the activity of stroma-free hemolyzates.

With regard to the TPN-malic enzyme, it should be pointed out that the activity of this enzyme in human arterial tissue is only about 2% of that found in previous studies for DPN-malic dehydrogenase (1, 5). The demonstration of a definite activity of TPN-malic enzyme in human arterial tissue may nevertheless be of importance, because this finding indicates that the malate shunt is operating in the tissue. A comparison of the TPN-malic enzyme activity of the human arterial tissue with that reported for the cattle lens (9) shows an activity of the lens which is approximately 4 times higher than that of the arterial tissue.

SUMMARY

Determinations were made of the isocitric dehydrogenase and TPN-malic enzyme activities of 70 samples of the descending thoracic aorta, 60 samples of the pulmonary artery, and 43 samples of the coronary artery obtained fresh at autopsy from individuals ranging in age from 0 to 85 years. The activity assays were performed by spectrophotometric determination of the rate of reduction of TPN, using, respectively, D-L-isocitrate and L-malate as substrates. In the case of the aortic and coronary artery samples the enzyme measurements were made separately on normal and arteriosclerotic portions of the same blood vessels.

The average isocitric dehydrogenase activities observed for normal aortic, pulmonary artery, and normal coronary artery samples, expressed

as millimoles of TPN reduced/ Gm. wet tissue/ hour, were respectively, 0.064, 0.071, and 0.084. The corresponding values found for TPN-malic enzyme were 0.0127, 0.0107, and 0.0124. The enzyme activities showed no certain variation with age, and no statistically significant differences were observed between the mean activities of arteriosclerotic and normal tissue portions of the same blood vessels.

The study has demonstrated the presence in human arterial tissue of two additional TPN-reducing enzymes and of the malate shunt.

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DARK ADAPTATION AS A FUNCTION OF AGE AND TIME: II. A DERIVATION*

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The purpose of this paper is to present a mathematical derivation of a model for representing dark adaptation as a function of age and time. Since the model was derived from experimental data, it is to be interpreted as an empirical one. In an alternative statistical study of the relationship of dark adaptation and age, McFarland and Fisher (13) stated that the dark adaptation curve itself could be described as inversely logarithmic and therefore represented by the general equation,

$$y = 10^{a+bx} + C \qquad (1)$$

where,

y = $\mu\mu$l luminance
a = initial level of dark adaptation
b = drop time [Drop time is generally taken to mean the amount of time required to reach some predetermined level of dark adaptation.]
x = time
C = the asymptote of the curve.

However, it is also possible to compute C (3, 13) by the formula,

$$C = \frac{P_1 \times P_2 - P_3^2}{P_1 + P_2 - 2(P_3)}, \qquad (2)$$

where,

P_1 = a given value of the curve early in time, say, the 6th minute
P_2 = a value on the curve late in time, say, the 30th minute
P_3 = a value on the curve midway between P_1 and P_2
C = the asymptote of the curve.

This method of calculating C, the asymptote of the rod curve, is generally applicable to calculating the asymptote of the cone curve as well.

Hammond and Lee (6) stated that the dark adaptation curve can be represented by,

$$\text{Log } I = a + b/t^2 \qquad (3)$$

where,

a = a constant, the general level of the curve at the asymptote
b = a constant, the rate of adaptation
t = the time in minutes from the cessation of the pre-adaptation light stimulus.

In previous investigations, the general procedure was to fit the data by using various formulae and then to identify such parameters as the curve intercept, cone-rod curve intersection, drop rate, asymptote of the cone curve, and the asymptote of the rod curve. But dark adaptation is a phenomenon that is known to vary relative to a number of conditions, of which age is one. It is now certain that as age increases the curve is displaced upward on the *y* axis. At the same time the cone and rod segments of the curve seem to pivot around their individual focal points near the intercept. The pattern of displacement is extremely orderly.

It is quite evident that, if the age variable is related to the dark adaptation curve in some lawful manner, then this function could be described mathematically. If this is so, then it should be possible to describe the age curve family. However, this has not been done.

Instead, at this juncture in the history of investigating dark adaptation as a function of age, conventional statistical methods in the study of the age factor were substituted for a more mathematical resolution of the dark adaptation time and age interaction. This approach established beyond a reasonable doubt that dark adaptation becomes a function of age. For instance, in 1955 McFarland and Fisher (13) used formula 2 for obtaining C and found a correlation of 0.895 between age and C. Since the sample of subjects used was composed largely of aircraft pilots who were, by the nature of their occupation, highly selected with respect to visual efficiency, a correlation of this magnitude would not ordinarily have been expected. This is because restricted range of samples tends to lower the magnitude of the conventional product moment r. The results, r =

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0.895, however, failed to support their inference, because this correlation was one of the highest ever discovered among physiological and psychological relationships.

However, the statistical approach did not fulfill the need for a mathematical model of the dark adaptation, time, and age relationships. Consequently, new data obtained by McFarland, Domey, Warren, and Ward (10) were examined, and a search for a general equation was initiated. A model was constructed which made possible the accurate prediction of the mean level of adaptation for any point on the time continuum as a function of age.

METHOD

Subjects.—There were 240 male subjects, 30 of whom were drawn from each of 8 decades ranging from the teen-age level through the age of 89. Previous studies have shown that there is no significant sex difference in the dark adaptation phenomenon. The total sample of 240 subjects was composed of persons taken from YMCA youth groups, college-age students, university faculty, taxi drivers, unemployed persons obtained from the USES Agency, and retired men living at home or in private institutions for the aged. All subjects were paid for their services, and subsequent to obtaining the data, over half the subjects in each decade were then offered and given a complete eye examination free of charge.

Apparatus.—The instrument (7) used throughout this study was the Hecht-Schlaer Adaptometer, which had been rebuilt and recalibrated by the manufacturer (O. C. Rudolph and Sons, Caldwell, New Jersey, Model No. 1, Serial No. 14). The research was conducted in three different cities in order to accommodate aged persons for whom traveling was difficult.

Procedure.—After each subject was seated in the experimental room, his left eye was covered by a patch, and his head was held steady in a head-chin rest. Vision was uncorrected. The lights in the dark room were turned off, and after a lapse of approximately one minute, the retina of the right eye was bleached by exposure to a standard 1600 millilambert incandescent light source for 3 minutes. At the end of the pre-test period, the subject was presented with a red fixation point 7 degrees right of center. The 1 degree violet light test stimulus (53.0% transmission at 405 mμ was then presented. The duration of each test flash of light was 1/5 of a second.

The first observation was made within 59 seconds after the termination of the pre-exposure light. Then, beginning with the second minute, one reading was taken every minute for the next 9 minutes, every two minutes for the next 6 minutes, and every 3 minutes for the following 24 minutes. Therefore, 21 observations were made in 40 minutes of dark adaptation.

RESULTS

The numerical results are presented in table 1 where $\log_{10}$ $\mu\mu$l luminance in the body of the table is given as a function of age and time. Figure 1, constructed from the data found in table 1, shows that the family of dark adaptation curves obtained as a function of age rises

TABLE 1. DARK ADAPTATION AS A FUNCTION OF AGE AND TIME $\log_{10}$ $\mu\mu$l LUMINANCE.

Time	Age							
	16–19	20–29	30–39	40–49	50–59	60–69	70–79	80–89
30 Sec.	6.9294	6.7803	6.9492	7.0310	7.0590	7.2065	7.4874	7.6174
1 Min.	6.4198	6.1635	6.3834	6.6640	6.7873	6.9382	7.2554	7.4248
2	5.9346	5.6547	6.0472	6.2884	6.4988	6.7261	7.0634	7.2458
3	5.6602	5.4286	5.8517	5.9818	6.2562	6.5894	6.9865	7.1198
4	5.5830	5.2672	5.8470	5.8701	6.1794	6.4937	6.9687	7.0748
5	5.3598	5.0480	5.4505	5.6762	6.9549	6.2732	6.7029	6.9006
6	5.0760	4.8323	5.1558	5.4246	5.6407	5.9269	6.2839	6.7056
10	3.8543	3.9493	4.1648	4.5095	4.8026	5.2064	5.7469	6.1104
16	3.2399	3.1413	3.4364	3.7780	4.2024	4.5028	4.9947	5.5511
22	2.8718	2.8450	3.0387	3.3346	3.7404	4.0360	4.6035	5.2667
28	2.6422	2.7193	2.8611	3.1334	3.4973	3.7451	4.2207	4.9015
40	2.4272	2.6029	2.6945	3.0159	3.3459	3.6419	4.1043	4.8055

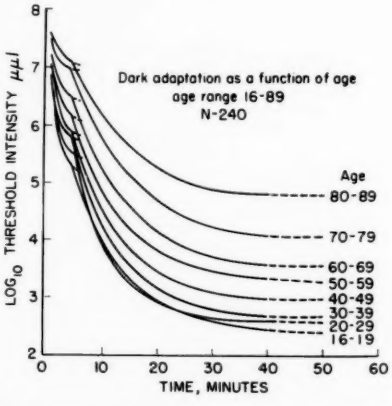

Fig. 1. Conventional dark adaptation curves showing the pronounced influence of age upon threshold of dark adaptation.

in an orderly manner, suggesting that the difference between their terminal point increases nonlinearly from one age level to the next. Since the curves for the 16-19-year-old group and the 20-29-year-old group seemed to be nearly alike, they have been combined for the purpose of simplifying the mathematical process which follows, although they are plotted independently in figure 1.

A Model for Dark Adaptation as a Function of Age.

For the sake of convenience in examining the level of dark adaptation as a function of age as well as time, the mean data have been replotted as time curves, as shown in figure 2. Here age has been entered on the x axis, and $\log_{10}$ $\mu\mu$l luminance entered on the y axis. Each individual curve in figure 2 represents the level of dark adaptation as a function of age at a given time in log units. It can be seen that the slope of the curves becomes greater as a function of age and time. When plotted in this way, the data appear as a family of positive exponential curves.

A suitable mathematical model of dark adaptation as a function of age and time was found to be,

$$\text{Log } y = G^{(Ct)^{f_1(A)}} \qquad \text{(Model A)}$$

The definition of the parameters will appear in the derivation. It will be seen that the form of the model for the cone family was identical with the form of the model for the rod family.

An examination of the graphic data in figure 2 suggests that it would be possible to fit each one of the curves independently. Since the hypothesis was that the family of curves seems to be an orderly function of age, constants common to all the curves were sought through several mathematical techniques. Such constants, if they could be isolated, would permit writing a mathematical expression of the decline with age of one important human function.

It was eventually discovered that a log log transformation of the original $\log_{10}$ $\mu\mu$l luminance curves shown in figure 2 resulted in reducing the distributions from curvilinear form to linear form. The straight line plots of the transformed data are shown in figure 3. The curves in figure 3 appear as reversed curves because the log log transformation values are negative. Hence the plots here reflect the sign of the numbers, not a change in function. Then, by the convenient method of least squares, the slope, m, and the constant, k, for each of the 7 rod curves were computed. The explanation will be in terms of rod curves. It is understood that the cone curves were treated

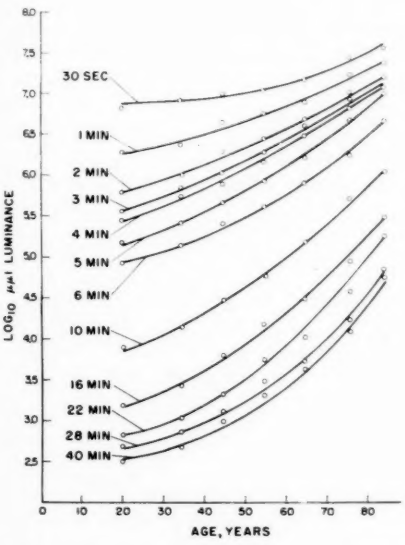

Fig. 2. Dark adaptation curves as a function of time plotted against age.

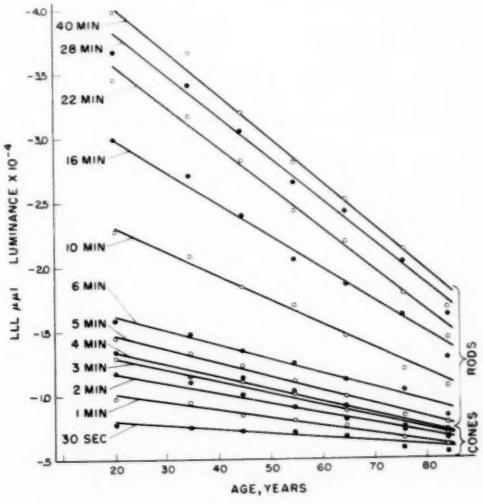

Fig. 3. Triple log transformation of dark adaptation as a function of time plotted against age. The result is a family of straight lines.

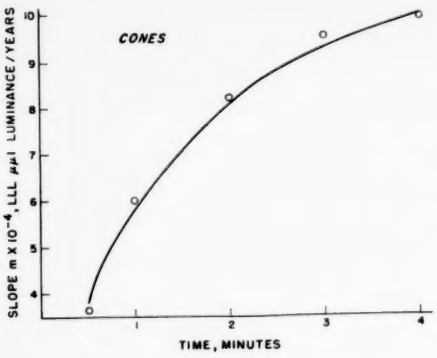

Fig. 4. The values of the first 5 slopes, (cones) shown in figure 3 plotted against time.

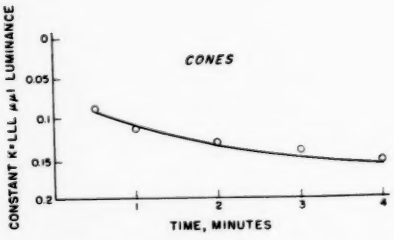

Fig. 5. The values of the constants of the first 5 slopes (cones) plotted against time.

in exactly the same manner. Now the method for treating all the time-age curves became self-evident. Thus, a plot of the derived slopes, m_1, m_2 . . . m_7 was made, as well as a plot of the derived constants, k_1 k_2 . . . k_7. The resulting curves of both the slopes, and the constants for both cones and rods appear in figures 4, 5, 6, and 7. It can readily be seen that deriving the formula for these second order curves would provide the constants necessary for constructing a mathematical model of dark adaptation as a function of the covariation of time and age.

Since these second order curves also were not linear, an appropriate transformation was also sought in order to simplify the mathematical treatment. It was discovered that the m_1, m_2 . . . m_7, and k_1, k_2 . . . k_7 plots could be reduced to linear form by a log-time transformation rather than by any transformation of the luminance parameter in these distributions. The success of this procedure can be clearly seen in figures 8, 9, 10, and 11. It followed once again that the application of the method of least squares to these transformed data would produce a slope-of-the-slopes, M_m, with its constant K_m. It would also yield a slope-of-the-constants, M_k, along with its own constant K_k. It was found that the first 5 but not the first 6 values of m and k could be fitted by the method described. It was also found that the last 7 but not the last 8 values of m and k could be fitted by the method described. Thus, the interval between the slopes and constants at the 4th-5th minutes defined the cone-rod transition point.

Since the data for cones and rods were plotted independently, there were duplicate expressions for both curves. Thus, M_m, M_k, K_m, and K_k represent the change in dark adaptation as a function of age and time, since they perform

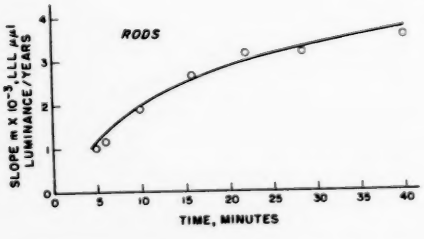

Fig. 6. The values of the last 7 slopes (rods) plotted against time.

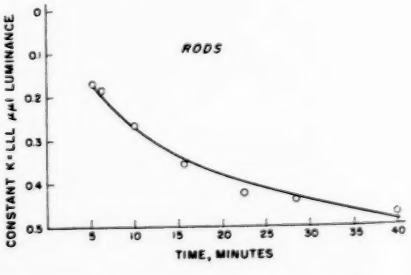

Fig. 7. The values of the constants of the last 7 slopes (rods) plotted against time.

the function of constants by tying all the curves together simultaneously. The coefficients for the cone equation are,

M_{mc}, slope of the slopes $= 7.189 \times 10^{-4}$

K_{mc}, constant of the slopes $= 5.94 \times 10^{-4}$

M_{kc}, slope of the constants $= -0.0750$

K_{kc}, constant of the constants $= -0.1111$

$\log t$, the time variable from zero time to infinity

A, the age variable from $x_1 \cdots x_\infty$

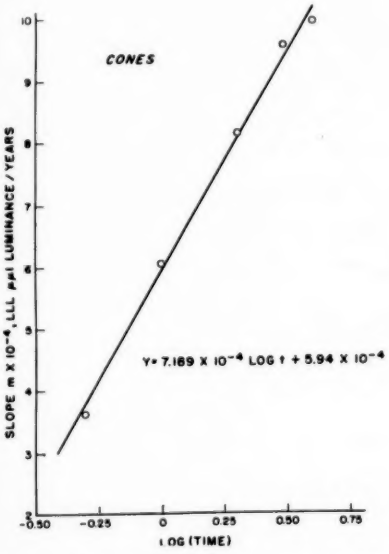

Fig. 8. Triple log transformation of the first 5 slopes (cones) plotted against log of time.

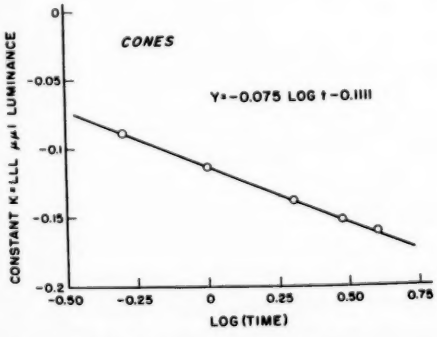

Fig. 9. Triple log transformation of the constants of the first 5 slopes (cones) plotted against log of time.

The coefficients for the rod equation are,

M_{mr}, slope of the slopes $= 29.52 \times 10^{-4}$

K_{mr}, constant of the slopes $= -9.785 \times 10^{-4}$

M_{kr}, slope of the constants $= -0.3640$

K_{kr}, constant of the constants $= +0.08814$

$\log t$, the time variable from zero time to infinity

A, the age variable from $x_1 \cdots x_\infty$

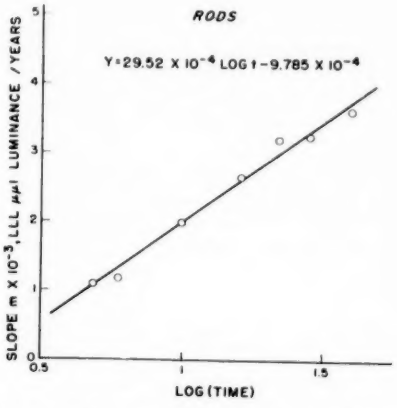

Fig. 10. Triple log transformation of the last 7 slopes (rods) plotted against log of time.

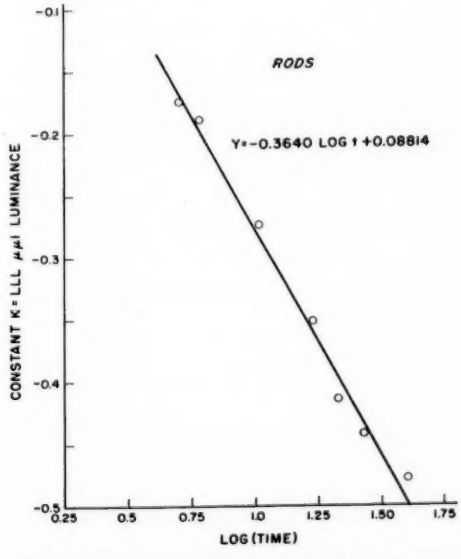

Fig. 11. Triple log transformation of the constants of the last 7 slopes (rods) plotted against log of time.

The complete explicit expression for the cones is

$$LLL_{10}\mu\mu l\ I = (7.189 \times 10^{-4} \times \log t + 5.94 \times 10^{-4})A - 0.0750 \times \log t - 0.1111$$

The rod curves can be represented by,

$$LLL_{10}\mu\mu l\ I = (29.52 \times 10^{-4} \times \log t - 9.785 \times 10^{-4})A - 0.3640 \times \log t + 0.08814$$

where A represents age, and t represents time. In explicit form the model for the cone curve appears in log $_{10}$ form as follows,

$$\text{Log } \mu\mu l\ I = 10^{10^{(5.94 \times 10^{-4}A - 0.1111)}\, t^{(7.189 \times 10^{-4}A - 0.0750)}}$$

The explicit form of the model for the rod curves is parallel, and is expressed as,

$$\text{Log } \mu\mu l\ I = 10^{10^{(-9.785 \times 10^{-4}A + 0.08814)}\, t^{(29.52 \times 10^{-4}A - 0.3640)}}$$

The explicit form of the model may be reduced to the general form in this way,

$$\begin{aligned} (1) \qquad LLL_{10}I &= (M_{mc} \log t + K_{mc}) \text{ Age} \\ &\quad + M_{kc} \log t + K_{kc} \\ &= AM_{mc} \log t + AK_{mc} \\ &\quad + M_{kc} \log t + K_{kc} \\ &= (AM_{mc} + M_{kc}) \log t \\ &\quad + (AK_{mc} + K_{kc}) \end{aligned}$$

Let

$$(2a) \qquad f_1(A) = AM_{mc} + M_{kc}$$

$$(2b) \qquad f_2(A) = AK_{mc} + K_{kc}$$

Substituting in equation (1),

$$(3) \qquad LLL_{10}I = f_1(A) \log t + f_2(A)$$

To express the equation entirely in terms of logarithms multiply $f_2(A)$ by log of 10, or 1.

$$(4) \qquad LLL_{10}I = f_1(A) \log t + f_2(A) \log 10.$$

Equation (4) is now reduced to the form

$$(5) \qquad \text{Log Log}_{10}\ I = 10^{f_2(A)}\, t^{f_1(A)}$$

To give the equation in logarithmic form multiply $10^{f_2(A)}\, t^{f_1(A)}$ by 1 or log of 10. Thus,

$$(6) \qquad \text{Log Log}_{10}\ I = 10^{f_2(A)} t^{f_1(A)} \log 10$$

$$(7) \qquad \text{Log}_{10}\ I = 10^{10^{f_2(A)} t^{f_1(A)}}$$

Referring to equations (2a) and (2b), $f_2(A)$ may be found as a function of $f_1(A)$ as follows:

$$f_1(A) = AM_{mc} + M_{kc}$$

$$A = \frac{f_1(A) - M_{kc}}{M_{mc}}$$

Substituting this value of A into equation (2b) leads to

$$f_2(A) = \frac{K_{mc}}{M_{mc}} (f_1(A) - M_{kc}) + K_{kc}$$

$$f_2(A) = f_1(A) \frac{K_{mc}}{M_{mc}} - \frac{K_{mc}M_{kc}}{M_{mc}} + K_{kc}$$

If the following substitutions are made for the constants, $f_2(A)$ may be reduced to a simpler form.

Let,

$$\frac{K_{mc}}{M_{mc}} = Z$$

$$K_{kc} - \frac{K_{mc}M_{kc}}{M_{mc}} = B$$

Then (2b) becomes

$$f_2(A) = Zf_1(A) + B$$

With this substitution equation (7) becomes,

$$(8) \qquad \text{Log } I = 10^{[10^{Zf_1(A)+B}][t^{f_1(A)}]}$$

Since 10^B and 10^Z are constants, the following substitutions may be made.

$$10^B = D$$

$$10^Z = C$$

Equation (8) is now

$$(9) \qquad \text{Log } I = 10^{DC^{f_1(A)} t^{f_1(A)}}$$

Since 10^D is a constant, the following substitution is possible,

$$10^D = G$$

Equation (9) may now be written as

(10a) $\text{Log } I = G^{cf_1(A)f_2(A)}$

(10b) $\text{Log } I = G^{(ct)f_2(A)}$ (Model A)

It can be seen that the determination of the boundaries of the derivation is dependent upon several parameters, (a) level of luminance, which cannot be zero, but must reach some least threshold value, (b) time in the dark which is not infinite except theoretically, since the (c) age range within which the dark adaptation phenomenon must exist must be more than zero and less than infinity. For practical and theoretical purposes it may be postulated that the range of luminance within which the model is estimated to be valid would be between approximately 1 year to 100 years, and a time in the dark period of approximately 60 minutes. Theoretically the dark adaptation curve is asymptotic. In reality any given dark adaptation curve could not exceed the life span of a subject. And in practical terms more than 98% of the dark adaptation curve is obtained within the first 60 minutes. Thus, luminance, age, and time values could never be zero or negative.

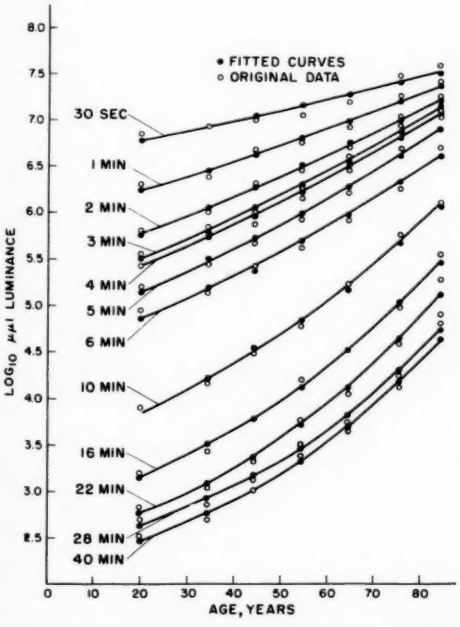

Fig. 12. Comparison of the original data as shown in figure 2 with the reconstructed data obtained from Model A. Model A is shown to fit the original data very closely.

In order to evaluate the derivation two procedures were devised.

Test Procedure 1.—In Procedure 1 mathematical Model A was used to reconstruct theoretical dark adaptation curves. Then the original data were compared with the theoretical constructs. Both sets of curves are exhibited in figure 12. While the dark adaptation level for the 80-89-year-old group was slightly overestimated, probably because of the concentration of several cataract defects found in persons who were at the far end of the age range, no serious challenge to the efficiency of the derivation was found. The correspondence of the predicted mean curves with the obtained mean curves is unusually close, so close, that one could be substituted for the other without doing violence to the interaction of the age-time covariables in the dark adaptation phenomenon. For instance, test re-test dark adaptation data usually vary by a displacement of half a log value. Model A fits the present data with far greater exactness.

Since the theoretical curves so closely resemble the original distributions, the model was considered valid for the obtained data. What remained was the need to test whether the model could be generalized, that is, extended to alternative independent samples. Test procedure 2 was designed to assist in evaluating this question.

Test Procedure 2.—A more rigid test of the generality of the equations would depend upon demonstrating that the model derived from one sample predicted the performance of other independent samples. The present data were treated in the following way to enable approximating the execution of such a test.

The second test procedure was divided into two parts, 1) one part for cone data, and 2) one part for rod data. The reason for treating cones and rods independently was to demonstrate that the stability of the model was not dependent upon the method of sampling.

Test Procedure 2a for Cone Data.—The principle of testing the mathematical model by deriving the data from one group and then predicting the performance of a second independent group was modified in the following way. It will be recalled that there were 8 age groups. They were assigned to two general classes, a criterion category, and a test category (table 2).

Then using only the data contained within the criterion group, a second model, Model B for cones, was derived independently from Model A. Therefore, there remained three independent test groups, the data from which did not enter into the construction of Model B, and thus could have in no way influenced the new Model. Special attention is called to the fact that the age ranges of the criterion groups are different from the age ranges of the test groups. Model B (cones) based upon only those scores inherent in the criterion groups was then compared with the original model, Model A, which was dependent upon all the sampled scores. A comparison of the several coefficients and exponents appears in the explicit formulae below.

Model A (cones). Original Model Inclusive of All the Data.

$$LLL_{10}\mu\mu l\ I = (7.189 \times 10^{-4} \log t - 5.94 \times 10^{-4})\ \text{Age} - 0.0750 \log t - 0.1111$$

Model B (cones). Second Derivation of the Model Inclusive of Only Those Data Obtained from the Criterion Group.

$$LLL_{10}\mu\mu l\ I = (7.282 \times 10^{-4} \log t - 5.73 \times 10^{-4})\ \text{Age} - 0.778 \log t - 0.1098$$

Clearly, the model for cones remained exactly the same with practically no changes occurring in the coefficients and exponents. In other words Model B can be substituted for Model A.

Test Procedure 2b for Rod Data.—In the procedure applied to rod data, the age groups were assigned to two categories, a criterion category and a test category, in the following way, as shown in table 3.

Then, using only the data contained within the criterion groups, that is, the middle 50% of the age range data, Model C for rods was constructed. There remained three independent test groups, all at the extremes of the age range distribution. The age category 16-29 contained 25% of the scores, and each of the age range categories, 70-79, and 80-89 contained 12.50% of the scores, respectively. Thus, half the data were used for deriving Model C for rods and half for test scores.

The comparison of the components of Model A with Model C for rods is as follows:

Model A (rods). Original Model Inclusive of All the Data.

$$LLL_{10}\mu\mu l\ I = (29.52 \times 10^{-4} \log t - 9.785 \times 10^{-4})\ \text{Age} - 0.3640 \log t + 0.08814$$

Model C (rods). Second Derivation of the Model Inclusive of Only Those Data Obtained from the Criterion Group.

$$LLL_{10}\mu\mu l\ I = (28.930 \times 10^{-4} \log t - 10.518 \times 10^{-4})\ \text{Age} - 0.3665 \log t + 0.09487$$

Once again there was no modification of the form of the model and practically no change in the coefficients and exponents larger than would be expected within rounding error.

It follows that Models B and C are virtually identical to Model A, not only in form but in coefficients and exponents as well. Since Model A fits the data with great fidelity so will Models B and C. Hence, Models B and C will predict the scores of their representative test groups, which are for the cone model the mean scores of age groups 30-39, 50-59, and 70-79, and which are for the rod model the means of the age groups 16-29, 70-79, and 80-89. Therefore, it has been established that the mathematical derivation of a model of dark adaptation as a

TABLE 2. AGE GROUPS FOR MODEL B.

Criterion Category (Cones) Decades	Test Category (Cones) Decades		
	(1)	(2)	(3)
16-29*			
	30-39		
40-49			
		50-59	
60-69			
			70-79
80-89			

* The 16-19, 20-29 age groups were combined, hence the enlarged range, 16-29.

TABLE 3. AGE GROUPS FOR MODEL C.

Criterion Category (Rods) Decades	Test Category (Rods) Decades		
	(1)	(2)	(3)
	16-29*		
30-39			
40-49			
50-59			
60-69			
		70-79	
			80-89

* The 16-19, 20-29 age groups were combined, hence the enlarged range, 16-29.

function of age and time represents (a) the original data and (b) predicts the performance of other independent groups of both the same or different age levels. Therefore, the model can be generalized.

In order to demonstrate the similarity among Models A, B, and C, the curves for all ages at time intervals 30 seconds, 2, 10, and 28 minutes have been calculated, using Models A, B, and C independently. Reproducing the entire range of curves for each model would be redundant, since any possible differences found among the models would remain constant, or approximately so, and thus would be as easily revealed at one time interval as another. The results appear in figure 13.

Rate of Dark Adaptation as a Function of Age.

Since there is now assurance that Model A can be generalized, an analysis of the relationship of rate of dark adaptation in terms of the model cannot be trivial. In order to simplify the mathematical technique in the following analysis, Model A has been used to derive rate of dark adaptation that would appear at the mean ages of 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100 years. The original data, through the use of the model, have simply been extrapolated to ages 10, 90, and 100 years. Since all the mean ages exist within the boundaries of the model, no mathematical rule has been broken when these are substituted for the actual mean ages, which are 19.7, 34.2, 44.3, 54.2, 64.2, 75.5, and 83.9.

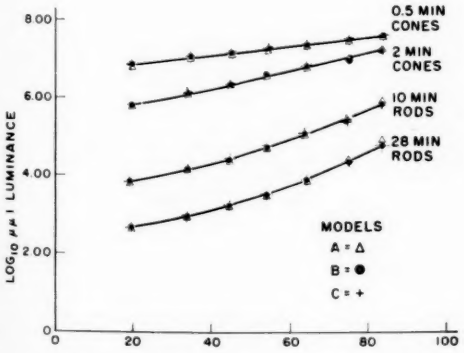

Fig. 13. Comparisons of Models A, B, and C.

The equation of the cone curve was differentiated in order to obtain an equation for rate of dark adaptation. Thus,

$$R = [G^{(Ct)^{f_1(A)}}]\left[\frac{(Ct)^{f_1(A)}}{t}\right] f_1(A) \ln G$$

The constants for the original equation, Model A, were applied to the cone curves and evaluated as follows:

$$Z = \frac{K_{mc}}{M_{mc}} = \frac{5.940 \times 10^{-4}}{7.189 \times 10^{-4}} = 0.8263$$

$$B = K_{kc} - \frac{K_{mc}M_{kc}}{M_{mc}} = -0.0491$$

$$D = 10^{B} = 10^{-0.0491} = 0.89309$$

$$C = 10^{Z} = 10^{+.8263} = 6.7035$$

$$G = 10^{D} = 10^{+.89309} = 7.8178$$

In an identical manner the constants for the original equation, Model A, were applied to the rod curves and evaluated as follows:

$$Z = \frac{K_{mr}}{M_{mr}} = \frac{-9.785 \times 10^{-4}}{29.52 \times 10^{-4}} = -0.3315$$

$$B = K_{kr} - \frac{K_{mr}M_{kr}}{M_{mc}} = -0.15$$

$$D = 10^{B} = 10^{-0.15} = 0.7080$$

$$C = 10^{Z} = 10^{-0.3315} = 0.4661$$

$$G = 10^{D} = 10^{0.7080} = 5.021$$

The data for rate of dark adaptation at the 30th second and the 6th minute for mean ages 10, 20 . . . 100 years will be found in table 4, and in figures 14 and 15. It can be seen that when the dark adaptation rate data were plotted as a function of age the resulting distributions were curvilinear. It was discovered that rate seemed to be part of a cosine function when plotted over the independent variable, that is, age. Thus, the age variable was divided by 10 and transformed into angular degrees in order to keep the data within the correct angular range, 0°-90°, when the data were evaluated. For cone data it was found that an additive constant, 17°, was necessary in the transformation equation. The constant, 17°, in ϕ_1 was determined empirically and is valid only for the experimental conditions described in this paper. This constant will have to be reestab-

TABLE 4. RATE OF DARK ADAPTATION.

Mean Age	Log_{10} $\mu\mu$l Luminance/Min.	
	Time, 30 Seconds	Time, 6 Minutes
10	−2.13237	−0.1241
20	−1.95500	−0.1208
30	−1.76747	−0.1[illegible]
40	−1.56913	−0.1114
50	−1.35980	−0.1051
60	−1.13860	−0.0973
70	−0.90500	−0.0881
80	−0.65833	−0.0769
90	−0.39790	−0.0636
100	−0.12346	−0.0480

lished when the conditions vary. The functions are shown as follows. For the rate at the 30th second the form for cones is,

$$\phi_1 = \frac{(\text{Age})}{10} + 17^0$$

$$\text{Rate} = a \cos. \phi_1 + h$$

where,

a = a constant, slope

h = a constant, the intercept

For the rate of adaptation of rods as a function of age at 6 minutes the transformation is,

$$\phi_2 = \frac{\text{Age}}{10}$$

$$\text{Rate} = a \cos. \phi_2 + h$$

The curvilinear form of the data and the linear transformation data are shown in figures 14 and 15. The success of the transformation is evident.

All that remained was the derivation of the equations which would express rate of dark adaptation as a function of age for cones and rods. It was equally clear that the equations for the two linear transformed slopes were the expressions showing the relationship between rate of dark adaptation and age. The slopes were computed by the method of averages in the following way. Each slope was divided into two segments and the values substituted into the equation $R = ab \cos \phi$. Since, for each curve, there were two segments with 5 values in each segment, the result was a total of 10 equations from which, by the addition of 5 different equations at a time, two equations involving the constants a and h were obtained. These, in turn, were solved simultaneously and the constants

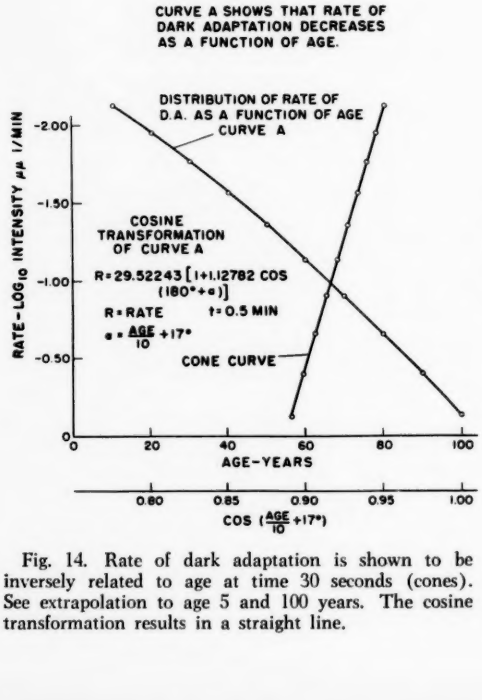
CURVE A SHOWS THAT RATE OF DARK ADAPTATION DECREASES AS A FUNCTION OF AGE.
DISTRIBUTION OF RATE OF D.A. AS A FUNCTION OF AGE CURVE A
COSINE TRANSFORMATION OF CURVE A
R=29.52243 [1+1.12782 COS (180°+ø)]
R=RATE t=0.5 MIN
ø = AGE/10 +17°
CONE CURVE
RATE-LOG10 INTENSITY μμ I/MIN
-2.00
-1.50
-1.00
-0.50
0
0 20 40 60 80 100
AGE-YEARS
0.80 0.85 0.90 0.95 1.00
COS (AGE/10 +17°)

Fig. 14. Rate of dark adaptation is shown to be inversely related to age at time 30 seconds (cones). See extrapolation to age 5 and 100 years. The cosine transformation results in a straight line.

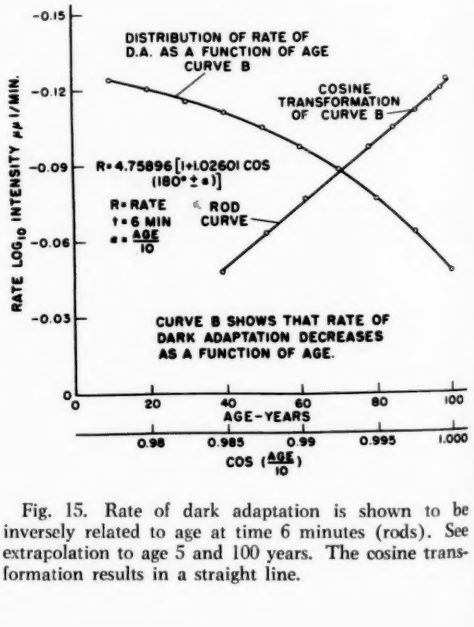
DISTRIBUTION OF RATE OF D.A. AS A FUNCTION OF AGE CURVE B
COSINE TRANSFORMATION OF CURVE B
R=4.75896 [1+L02601 COS (180°±ø)]
R=RATE t=6 MIN ø = AGE/10
ROD CURVE
CURVE B SHOWS THAT RATE OF DARK ADAPTATION DECREASES AS A FUNCTION OF AGE.
RATE LOG10 INTENSITY μμ I/MIN.
-0.15
-0.12
-0.09
-0.06
-0.03
0
0 20 40 60 80 100
AGE-YEARS
0.98 0.985 0.99 0.995 1.000
COS (AGE/10)

Fig. 15. Rate of dark adaptation is shown to be inversely related to age at time 6 minutes (rods). See extrapolation to age 5 and 100 years. The cosine transformation results in a straight line.

evaluated. The resulting equations for cones and rods are given below.

For cones at 30 seconds and rods at 6 minutes,

Cone Rate

$$= 29.52243\ [1 - 1.12782 \cos (180° + \phi_1)]$$

Rod Rate

$$= 4.75896\ [1 - 1.02601 \cos (180° + \phi_2)]$$

Since ϕ_1 and ϕ_2 contain the age variable, rate will change as ϕ_1 and ϕ_2 change. It follows that dark adaptation is a lawful function of age.

DISCUSSION

It has been demonstrated that dark adaptation threshold is extremely sensitive to vitamin A deficiency (8), hypoglycemia (12), and anoxia (11) and that the dark adaptation threshold becomes a lawful function of age (13). One inference supported by this type of finding is that dark adaptation is dependent upon fundamental physiological processes, such as sugar metabolism, oxygen transport, and utilization. Since it is known that metabolic processes also change with age, the modification of dark adaptation threshold with age is consistent with the inference. For instance, Boothby, Berkson, and Dunn (2), and Lewis, Duval, and Iliff (9) have all shown that oxygen consumption per unit of surface area declines with age. It has been indicated by Shock (15) that age and metabolic rate are inversely related. Also, the dark adaptation threshold is directly influenced by oxygen deprivation.

Since it has been shown that dark adaptation threshold and age are directly related and that physiological processes of which dark adaptation is a function in turn are related to age, then it would be expected that rate of dark adaptation would also vary, that is, decrease as chronological age increases. However, experimental evidence for a change in rate of dark adaptation relative to age is insufficient. Thus, Friedenwald (5) stated that there was a positive correlation between age and rate of dark adaptation, but the evidence in the source he cited (4) was inadequate. In this presentation the data were given in table and graphic form but no statistical evidence showing that age and rate were correlated was included. Hammond and Lee (6) showed that the correlation between age and an indirect measure of dark adaptation, that is, drop time, was correlated -0.06 with age. McFarland and Fisher (13) obtained a correlation of -0.13 with drop time and age. These values are no greater than chance would allow. Pinson's (14) findings are in the opposite direction, since he discovered that the area subtended by the dark adaptation curve for younger subjects was greater than the area subtended by the dark adaptation curve for older subjects.

Since the original individual scores obtained by Pinson were not included in the study, no independent statistical analysis could be devised to test his conclusion. Birren and Shock (1) have asserted that there is no correlation between age and rate of either cone or rod adaptation. The present study showed that rate of dark adaptation and age were inversely related. This supported Pinson's original position.

Thus, the evidence concerning the relationship between age and rate of dark adaptation is either negative or equivocal. This implies that the photochemical cycle remains unchanged with age, which in itself seems to be unlikely since the dark adaptation threshold decreases with age, and because other physiological processes do not remain constant with age (15).

In an attempt to resolve this dilemma, the sources cited above were subjected to a close textual analysis in order to discover whether the methods previously used for isolating the rate variable were self-defeating. It was found that most studies presenting chance correlations of age with rate of dark adaptation depended upon a substitute parameter called drop time. This is not an especially useful measure because (a) drop time is linear and therefore cannot actually represent true rate in the non-linear dark adaptation curves, and (b) drop time is itself dependent upon the displacement of the dark adaptation threshold and it is this dependence which is the primary phenomenon of dark adaptation in the aged. Birren and Shock (1) have called attention to this co-variation and have objected to it for the same reason. Finally, McFarland and Fisher (13) noticed that drop time seemed to be curvilinear with age. They found that when drop time was used as a criterion the rate of dark adaptation as a function of age was U-shaped. The method of describing this relationship utilized in this paper

shows that rate of dark adaptation, although curvilinear, varies inversely with age.

In the study presented by Birren and Shock (1) it was found that other measures were employed in the analysis of rate adaptation in a variable age sample. These investigators asserted that there was no correlation between age and rate of dark adaptation. In order to evaluate the evidence it is necessary to cite (1) the way in which the data were treated. Thus,

> The values for each subject were plotted on log-log paper in duplicate. Two investigators made independent graphic fits for each portion of the characteristic dark adaptation curve. The slopes of the graphic linear fit on the log-log paper were computed for each subject. Two independent estimates of the rate of cone and rod adaptation were thus obtained. The correlation between the slopes estimated by the two investigators was 0.90 + or — 0.02 for both cone and rod adaptation rates. The means of the two independent determinations were used as the best estimate of the rates of adaptation for each subject.
>
> The data were then analyzed to determine the correlation between the following variables: cone rate, 6 minute threshold, rod rate, 26 minute threshold.
>
> . . . . . .
>
> There was no correlation between age and either rate of cone adaption or rate of rod adaptation.

The log-log transformation evidently was made in order to convert the original dark adaptation data to linear distributions. The present investigators demonstrated that, in order to transform complete dark adaptation curves to linear plots, it was necessary to convert micro-microlamberts through three successive log transformations and then to plot the resulting data against log time. Thus, on the ordinate (y axis) will be plotted log-log-$\log_{10}$ $\mu\mu$l luminance; when the abscissa (x axis) is in $\log_{10}$ time units.

Since this is not what Birren and Shock (1) did, and because the partially transformed data were fitted by eye, the fitting error could be considerable. And while it was said that the slopes of the graphic fits were computed, it must be realized that the slopes were not first computed from the transformed data and then plotted, but instead the values of the slopes were read from the graph after the data had been plotted by eye.

In addition it was said that there was a tendency for the transition time between cone and rod vision to be greater in the aged, since r between time of transition and age was 0.47, a significant correlation. Other studies (13, 14) have shown that transition time is independent of age in samples of healthy subjects. However, the shift in transition time along the abscissa (the x or time axis) does appear repeatedly in the dark adaptation curves of persons suffering from cirrhosis of the liver and the typical vitamin A deficiency associated with this disease. One is reminded that the subjects in the Birren and Shock sample were ambulatory, indigent, middle-aged, and elderly persons (ages 40-83). The possibility of nutritional disorders could be higher in such a sample than in one drawn from the general population. This observation does not by itself demonstrate that such was the case. Nonetheless, the adequacy of the sample for testing the hypothesis is not demonstrably unqualified.

It is also evident that if cone-rod transition time was actually significantly greater for the older than for younger subjects, then it must follow that rate of adaptation was less rapid for the aged than for younger persons. This inference would obviously be contradictory to the main conclusion that adaptation rate and age are uncorrelated. However, Birren and Shock specifically state that this datum cannot be used as evidence for an altered rate of adaptation in the aged because, ". . . there exists the possibility of an older subject possessing a combination of low cone threshold and a high rod threshold."

This entire analytic progression now encloses a circular argument, since it has led directly to the assumption that a low threshold for cones and a high threshold for rods must perforce be independent of the rate at which threshold sensitivity varies in each. It is just as easy to assume that there exists the possibility of a younger subject possessing a combination of high cone threshold and low rod threshold. Or, in the absence of evidence, it could be argued with equal force that this hypothetical shift was not due to threshold at all, but actually did reflect the difference in rate of adaptation between the aged and the less elderly persons.

There is a consequence inherent in denying that delayed transition time in the aged, due to a difference of cone-rod threshold, can be used as an indicator of differential dark adaptation rate. First of all this denial depends upon assuming that adaptation rate and threshold are indeed independent in healthy subjects. But since this is the hypothesis being tested, it cannot appear as its own premise.

This elliptical argument must end in the following way: if the difference in transition time is real, and if the source of the difference is unknown, then, since the several subjects were not matched for equivalent transition times within the several age categories, there must be an uncontrolled variable contributing to the

statistical significance of the correlation between age and rate of transition. On the other hand, the cone and rod thresholds and the various transition times were variables inherent in the estimation of the graphic fit slopes from which the primary measures of rate of dark adaptation were extracted in this experiment. Since all this is true, then the experiment is confounded and the conclusions void.

Other observations are as follows. Since 20 scores were obtained from each subject at specified times, then all the mean curves should contain 20 plotted points, and they do. However, the mean curve for the younger subjects has been plotted with two mean scores at the 8th minute and no mean score at the 9th minute, as shown in the curves for the two older groups. It is probable that the lesser of the two scores plotted at the 8th minute should have been plotted at the 9th minute.

In table 2 in Birren and Shock's paper the correlation between age and rate of dark adaptation is shown to be 0.24. When N is as large as 86, a correlation of this magnitude is statistically significant between the 0.05 and 0.01 level of confidence. This seems to be at variance with the main conclusion that rate of dark adaptation and age are unrelated.

The review of the literature shows that evidence regarding the relationship of rate of dark adaptation and age is unclear. Therefore, the present study has tended to clarify the uncertainty in the literature and has added quantitative data toward the solution of the relationship between the thresholds and the rate of dark adaptation as a function of age.

SUMMARY

In order to describe one family of dark adaptation curves obtained from an age sample of 240 men, ranging from 16 through 89 years, a mathematical model of the form

$$\log y = G^{(Ct)^{f_1(A)}}$$

was derived.

It was found that the model could be generalized. In addition it was concluded that threshold of dark adaptation as a function of time was lawfully related to chronological age.

Rate of adaptation was determined by differentiating the equation at 30 seconds and 6 minutes as follows,

$$R = [G^{(Ct)^{f_1(A)}}]\left[\frac{(Ct)^{f_1(A)}}{t}\right] f_1(A) \ln G$$

The results showed that rate of dark adaptation was a curvilinear function of age.

These findings are consistent with the hypotheses that the thresholds and rate of dark adaptation depend upon basic underlying physiological processes that change with age.

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BOOK REVIEWS

THE ARTERIAL WALL. AGING, STRUCTURE, AND CHEMISTRY, edited by Albert I. Lansing, The Williams & Wilkins Co., Baltimore, 1959, 259 pages, $7.50.

One charming thing about the book is the introduction by Dr. Lansing, more particularly the last paragraph, which consists mainly of provocative questions.

Woemer's article concerning the relation of the vasa vasorum, or lack of relation, to the intima suggests strongly that injury or disease of the intima precedes vascularization and that vascular lesions of the intima are the result rather than cause of the pathological picture.

Zweiback's review is spotty and diffuse in bringing up various examples of reactions and functions of endothelial cells. Although it is confusing, this very fact may serve to stimulate better morphological and biochemical studies of endothelial tissue.

Mommaerts' monograph called Perspectives in the Study of Arterial Muscle has, as he stated at the outset, less to do with the muscular coats of arteries than anyone could imagine. It is, however, a very thorough and interesting, even though a very wordy, review of what is known about the chemical nature of the proteins in striate muscle and their relation to function, namely to the phenomenon of contraction. The sidelong glance at "Smooth Muscle" does not seem to add much because of the paucity of published material — Mommaerts seems to feel the same way. It is unfortunate that he uses so many words to refer to what he is going to write about in the "next section"; but perhaps this was necessary for continuity. However irrelevant to anything known about the arterial wall, the article is stimulating in the sense that it points out how miniscule our knowledge of the musculature of the arterial wall is. Every reader cannot but be grateful for the unusual excellence of the bibliographies appended to this monograph.

Bachelor and Leven's chapter on collagen seems to the reviewer to exhibit some of the traits of the previous one—wordiness, speculation, prophecies of future successes but very little substance. I could not be clear as to what the "present study" mentioned first on page 113 and frequently thereafter was, unless it was that tissue structure and movement of fluids were interrelated. The whole article seemed to be one of indirection without presentation of any evidence. Perhaps this sort of presentation is good in that it points out how small is the amount of concrete knowledge concerning the relationship between movement of fluids and the structure and composition of tissues.

Lansing's chapter on elastic tissue is a well-assembled discussion of the various means of distinguishing between collagen and elastin, together with sparse evidence that both derive from fibroblasts. The differences between the two tissues based on staining properties, microscopic appearance, chemical composition, and biological properties are made about as clear as present knowledge permits. It is good to have this knowledge so clearly assembled. Changes with age as well as controversies concerning these changes are also ably presented. The discussion of elastase, a difficult assignment at this stage, went just about as far as present circumstances permit.

The chapter concerning the mucopolysaccharides by Kirk is pure delight. The citations of literature on the subject is extremely useful and, considering the large part that Kirk has played in the field of the mucopolysaccharide content of arterial walls, he is extremely modest. When one considers the immense amount of work which Kirk and his associates have done in an effort to show whether or not changes with age occurred, the fact that his group was, for the most part, unable to show changes with age, in other words negative results, is precisely the information we need.

The results gibe with those of Lowry and Hastings, who showed that there was little if any change in cellular water content with aging. The speculations as to the function of the mucopolysaccharides in the arterial wall are succinct.

Barrows and Chow present the problem of the presence of various sorts of enzymes in the arterial wall quite carefully and conclude that an unbalance of enzymes systems, rather than a general decrease in activity, occurs during the process of aging. The bibliography is excellent, especially for students in the field.

Boucek and Noble present a very concentrated review of the current information concerning the ability of connective tissue to synthesize cholesterol or "sterols" and show that this ability varies with different species. The possible relationship of lipid metabolism of the fibroblasts to vascular changes with age is suggested. The present reviewer would like to know something about sphyngomyelin formation since this substance increases so markedly in arteries with age and with arteriosclerosis.

Lehninger's essay on the metabolism of the arterial wall is perhaps one of the most lucid discussions that has appeared on this subject. The various morphological entities are carefully described, and in turn the various chemical transformations and synthesis are elucidated. Particularly useful is the separation of the major metabolic processes for "housekeeping" of the cell from the specific metabolic processes necessary for particular functions, e.g., contraction, enzyme secretion, etc. The author suggests that the views he presents are "analyzed . . . from some distance." The value of the look at the arterial wall from the height of biochemical knowledge is at once apparent. It is a very enlightening description of the possibilities of biochemical reactions which may take place in the arterial wall.

SUBSCRIPT

Had I read the summation by Abraham Dury before I wrote this Review, I would have probably decided it was not necessary to write one. His summation of the origin and purpose of this publication is a very orderly and instructive one.

I have in the preceding paragraphs taken up each Chapter separately and now must only add emphasis to Dury's remark that it was his hope and that of Mr. F. D. Dorn that this volume would bring to light the scant evidence concerning the functions of the arterial wall as an organ of the body and hence stimulate interest in furthering knowledge of the very complicated role the arteries play in body economy. Not only does the musculature of the arterial wall serve to regulate

arterial pressure and distribute the output of blood from the heart to the varying needs of the organs of the body but it also plays a role in the biochemical synthesis of various substances, lipid, carbohydrate, and perhaps protein.

Actually the knowledge about the arterial wall itself seems so limited that the authors have been forced, for the most part, to reason by analogy from studies of tissue other than the arterial wall. It is a good sign that interest in this particular organ of the body has at least been established.

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PATTERNS OF INCIDENCE OF CERTAIN DISEASES THROUGHOUT THE WORLD: OPPORTUNITIES FOR RESEARCH THROUGH EPIDEMIOLOGY. Prepared for the Committee on Government Operations, United States Senate and its Subcommittee on Reorganization and Internal Organization, U. S. Government Printing Office, Washington, D. C., November 9, 1959, 54 pages, paper bound, 20 cents.

Primarily this publication was used to provide background information to the Subcommittee during its international health study. It is the sixth publication in a series of such reports.

Part of the report is an extensive evaluation of the level of activity and the need for epidemiology at an international level. Again and again the report recognizes a great lag in the amount of epidemiological work in process as compared to the many opportunities and the great need for such research that exists.

The report recognizes a number of significant changes in the twentieth century world, including a tremendous increase in rapidity of transportation, increase in radioactive sources of energy, new methods of infectious disease control, increase in world population accompanied by even greater increases in numbers of older people, and the emergence of chronic disease as an important health factor. It is postulated that these factors have important effects on the science of mass phenomena of diseases and human defects. Historically the emphasis has been on communicable and infectious disease and this indeed continues to be an important epidemiological pursuit. However, the rapid change to prevalence of chronic diseases along with increased life expectancy, clearly points out the increased importance of epidemiology of aging and of degenerative disease.

Specifically in regard to aging the report recognizes that a great deal more effort is needed in basic research in biological, clinical, behavioral, and social sciences. The need for greater effort in basic research and especially in genetics is recognized in all areas, however.

The World Health Organization is seen as uniquely qualified to spearhead epidemiological research. Many basic vital statistics and health records need to be standardized and extended to the large portion of the world's population which do not now have them. The report states that "only 33 per cent of the total number of deaths was registered in 1951 to 1955. The proportion of deaths of which the cause is known is far smaller still."

A major portion of the report is devoted to a selective description of world-wide opportunities for epidemiological research by disease category—cancer, heart disease, diabetes, arthritis, sickle cell anemia, peptic ulcer, dental diseases, mental illness, and neurological disorders are selected. In each instance a brief review of pertinent current epidemiological knowledge is given. An impressive array of etiological factors or partial factors has been brought to light by epidemiological research methods in many of these diseases. The report clearly and convincingly documents the great value of these methods in bringing to light etiological clues which can be tested and refined in a laboratory and fairly promptly brought to the level of therapeutic or public health control measures.

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BOOKS RECEIVED

Biochemistry of Human Genetics. Ciba Foundation Symposium, edited by G. E. W. Wolstenholme and Cecilia M. O'Connor, Little Brown & Co., Boston, 1960, 347 pages, $9.50.

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Section B

Psychological and Social Sciences, Social Welfare

Edited by

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Bernice L. Neugarten, Ph.D.

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VOLUME 15, SECTION B JULY, 1960 NUMBER 3

THE EFFECT OF AGE ON THE INTELLECTUAL PERFORMANCE OF MENTAL DEFECTIVES*

ANNE BELL, M.A., AND JOHN P. ZUBEK, Ph.D.
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The purpose of this investigation was to study the effect of age on the intellectual performance of familial mental defectives. A review of the literature showed that few of the many studies concerned with the relationship between age and intellectual processes dealt specifically with the lower intelligence range. Furthermore, almost all of the relevant research has been on children and adolescents and has largely utilized the Stanford-Binet test (Cattell, 1931; Doll, 1920; Kuhlmann, 1921; Sloan & Harman, 1947). The only extensive work on mental defectives covering a wider span of life was performed by Thompson (1951) on a group of 137 subjects aged 16 to 69 years. Unfortunately, however, Thompson studied only a handful of older subjects, and most of the tests employed were performance tests. The only other relevant studies were carried out by Clarke and Clarke (1954) and Clarke and Reiman (1958) on young adults who were given the Wechsler test. These studies will be taken up in some detail in the discussion section of this paper. In view of this paucity of data it was felt that it would be worthwhile to appraise the performance of mental defectives on the Wechsler-Bellevue test in the age range of 15 to 64 years.

PROCEDURE

The subjects were 100 patients at the Manitoba School for Mentally Defective Persons. Five years previously they had all been given the Wechsler-Bellevue Intelligence Scale (Form I). At that time they were divided into four groups of 25 subjects each in such a manner that the mean age of the groups approximated 20, 30, 40, and 50 years of age. In order to control for initial intellectual capacity, the four groups were so selected that their mean raw scores on the Wechsler Vocabulary Test were approximately the same (Mean = 8.05). Performance on a vocabulary test is generally considered to provide a fairly reliable index of a person's original intelligence level since vocabulary level is highly correlated with general intelligence and furthermore shows little or no decline with age. All of the subjects had been diagnosed as familial cases. Other diagnostic categories of mental defectives were excluded.

With the exception of eight cases, all of the patients had been in the institution for at least a year before the Wechsler test was administered. It was felt that an allowance of at least this time interval would result in a more valid set of scores, for by that time any of the problems arising out of the institutional process itself would have had an opportunity to resolve themselves, and the physical and mental effects of any adverse early environment could have been overcome to some extent by medical treatment and by social and emotional support. Insofar as possible, the four groups were so selected that their early, pre-institutional environments were essentially the same. Very few of the cases could be said to have come from very adverse early environments.

Five years later, when the mean ages of the four groups were approximately 25, 35, 45, and 55 years, the subjects were again given the Wechsler-Bellevue Intelligence Scale (Form I). Approximately a quarter of both tests and retests in all age groups were administered by the same psychometrician. The remainder of the testing was done by two other psychometricians.

Table 1 summarizes the data on the four groups of subjects at the time of the initial test. It can be seen that on the basis of mean IQ,

* The writers wish to express their appreciation to the National Research Council of Canada for the financial support of this study. They also wish to express their gratitude to Dr. H. S. Atkinson, Superintendent, The Manitoba School, for his kindness in placing the facilities of the institution at their disposal and to Dr. R. Gibson and Miss Lois Fry for their assistance at various stages of the study.

all four groups fall in the moron category of the mental defective population.

RESULTS

The findings of this study will be presented under two main headings: first, test-retest results; second, long-term age trends.

Test-retest

Changes in IQ. Table 2, Part A, shows the IQ scores obtained by the four age groups on the Full, Verbal, and Performance Scales of the Wechsler. It can be seen that on the Full Scale all age groups showed a significant gain on the retest. The mean gain ranged from 9.1 points for the youngest group to 4.4 for the oldest. From the table it is evident that individual differences in performance are large, with some subjects showing a decrease of a point or two in IQ and others showing gains as high as 22 IQ points. One of the surprising findings was the sizeable number of the oldest subjects who showed gains of 10 points or more.

On the Verbal Scale, all age groups again showed a significant gain in IQ on the retest. The differences in mean gain were quite small, ranging from 4.1 points for the youngest age group to 4.4 for the oldest. Individual differences were again quite large, ranging from a loss of 6 IQ points to a gain of 17. The magnitude of the individual differences is very similar in the different age groups with the exception of the youngest group where it is somewhat larger.

On the Performance Scale, all age groups except the oldest showed a significant gain in IQ on the retest. The largest mean gain (12 points) was made by the youngest group. The gain of 1.7 points obtained by the oldest age group was not significant ($t = .97$, $p > .10$). This is due to the fact that as these subjects now ranged in age from 50 to 69 years, they received

TABLE 1. DISTRIBUTION OF 100 SUBJECTS BY AGE, SEX, LENGTH OF INSTITUTIONALIZATION AND IQ AT TIME OF INITIAL TEST.

Group	Age		Sex		Years in Institution		I Q on Initial Test		
	Range	Mean	M	F	Range	Mean	Range	Mean	*S D*
I	15–24	20.2	11	14	1–13	4.3	43–83	55.4	4.75
II	25–34	30.2	17	8	0–25	10.4	45–86	60.0	5.96
III	35–44	39.6	10	15	0–38	15.2	49–87	65.2	4.81
IV	45–64	51.1	11	14	0–40	17.7	56–78	66.3	3.16

TABLE 2. MEAN TEST-RETEST CHANGES ON THE WECHSLER FOR FOUR AGE GROUPS OF MENTAL DEFECTIVES.

Age Group[a]	Full Scale				Verbal Scale				Performance Scale			
	Test	Retest	Mean gain	Range	Test	Retest	Mean gain	Range	Test	Retest	Mean gain	Range
					A: IQ Scores							
I	55.4	64.5	9.1[c]	3 to 22	58.2	62.3	4.1[c]	−6 to 17	60.8	72.8	12.0[c]	0 to 33
II	60.0	67.6	7.6[c]	−1 to 15	60.6	64.8	4.2[c]	−4 to 12	64.9	74.2	9.3[c]	−1 to 28
III	65.2	70.9	5.7[c]	−2 to 13	65.4	69.7	4.3[c]	−2 to 11	70.3	77.7	7.4[c]	−4 to 22
IV	66.3	70.7	4.4[c]	0 to 16	65.8	70.2	4.4[c]	−2 to 13	72.5	74.2	1.7	−5 to 10
					B: Scale Scores							
I	36.7	44.7	8.0[c]	−1 to 26	13.9	15.7	1.8[b]	−5 to 13	22.8	29.0	6.2[c]	−1 to 22
II	32.9	38.9	6.0[c]	−6 to 17	13.3	15.9	2.6[c]	−2 to 9	19.6	23.0	3.4[c]	−5 to 18
III	31.1	36.1	5.0[c]	−5 to 17	14.3	16.5	2.2[c]	−3 to 8	16.8	19.6	2.8[c]	−5 to 15
IV	23.4	27.6	4.2[c]	−4 to 12	10.1	13.1	3.0[c]	−4 to 10	13.3	14.5	1.2[b]	−4 to 8

[a] Mean age at time of retest: Group I, 25.0; Group II, 35.4; Group III, 44.6; Group IV, 56.0.
[b] Significant at the .02 level.
[c] Significant at the .01 level.

no additional allowance for aging above that received on the initial test, for Wechsler gives no credit in his tables above age 49. Their increase, although small, is entirely due to better actual performance. Individual differences in scores obtained are considerable, ranging from — 5 to 33 IQ points.

Changes in scale scores. Table 2, Part B, shows the scale scores obtained by the four age groups on the Full, Verbal, and Performance Scales of the Wechsler. In contrast to IQ scores, which reflect the allowances made for normal aging processes, scale scores show the subject's actual achievement at a particular age. It can be seen that on all three scales, all of the age groups showed a significant gain in scale scores on the retest. Individual differences in performance, as in the case of IQ scores, were again large.

Performance on subtests. Table 3 shows the test-retest changes on the six Verbal and five Performance subtests of the Wechsler. It can be seen that all age groups when retested showed either a significant gain or no change on all six Verbal subtests. On no subtest was there a significant decrement in performance. Comprehension showed a significant gain in all age groups; Vocabulary, in all age groups except the oldest; in Similarities the gain was significant only in the two oldest groups. Digit Span showed significant gains in age groups II and IV, while Information showed a significant gain only in the youngest age group (group I). Arithmetic exhibited no statistically significant change in any age group.

Table 3 shows that, with one exception, all age groups when retested showed either a significant gain or no change on the five Performance subtests. The one exception was Digit Symbol which exhibited a significant decrement in the oldest age group. The table also shows that Picture Arrangement improved significantly in all age groups except the youngest; Object Assembly in all but the oldest; and Picture Completion in all but group III. Block Design showed a significant gain in only groups I and II, while Digit Symbol showed a significant improvement in only the youngest group.

Individual differences. It was reported earlier that individual differences in performance on the retest were quite large. Table 4 shows the percentage of subjects in the different age groups who recorded a gain, no change, or a loss in scale scores at the retest. It will be noted that on the Full Scale, 88 per cent, on the Verbal Scale, 80 per cent, and on the Performance Scale, 81 per cent of all the subjects made gains or equalled their former scores. This superior performance on the retests is characteristic of all age groups, including the oldest. What is most surprising is the excellent performance of the subjects in the oldest age group, who at the time of the retest ranged in age from 50 to 69 years. Of this age group, 64 per cent surpassed their initial scores on the Full Scale, and another 16 per cent equalled them. A similar

TABLE 3. TEST-RETEST CHANGES ON SIX VERBAL AND FIVE PERFORMANCE SUBTESTS OF WECHSLER (SCALE SCORES).

Subtests	Age group							
	I		II		III		IV	
	Test	Retest	Test	Retest	Test	Retest	Test	Retest
Verbal:								
Comprehension	4.00	4.76[b]	3.80	4.64[c]	4.28	5.52[c]	3.00	4.40[c]
Vocabulary	4.16	4.52[b]	3.76	4.40[b]	4.20	4.72[c]	3.80	4.08
Similarities	2.36	2.56	2.36	2.84	2.54	3.16[c]	1.64	2.08[b]
Digit Span	2.76	2.36	2.20	2.76[a]	2.24	2.52	0.64	1.28[b]
Information	2.72	3.44[c]	2.88	3.28	3.12	3.40	2.76	2.96
Arithmetic	0.56	1.00	0.72	0.84	0.52	0.56	0.31	0.72
Performance:								
Picture Arrangement	3.80	4.12	2.88	3.64[c]	3.12	3.56[a]	2.24	2.68[a]
Object Assembly	6.32	7.92[c]	4.72	5.80[a]	3.92	4.92[b]	3.52	3.76
Picture Completion	4.20	5.52[c]	4.64	5.56[a]	3.48	4.00	2.48	3.52[c]
Block Design	3.76	5.08[c]	4.28	4.68	3.04	3.76[c]	3.00	2.96
Digit Symbol	4.68	6.32[c]	3.08	3.32	3.24	3.32	2.04	1.60[a]

[a] Difference significant at the .05 level.
[b] Difference significant at the .02 level.
[c] Difference significant at the .01 level.

TABLE 4. PERCENTAGE OF SUBJECTS SHOWING A GAIN, NO CHANGE OR A LOSS IN SCALE SCORES AT RETEST.

Age group	Full scale			Verbal scale			Performance scale		
	Gain	No change	Loss	Gain	No change	Loss	Gain	No change	Loss
I	84	12	4	48	28	24	88	8	4
II	80	8	12	68	16	16	68	8	24
III	84	4	12	68	12	20	68	8	24
IV	64	16	20	68	12	20	52	24	24
Mean	78	10	12	63	17	20	69	12	19

excellent performance was shown on both the Verbal and Performance Scales.

When an analysis is made in terms of IQ scores rather than scale scores, the percentages are even higher. This is because of the age increment allowed in the IQ scores by Wechsler. For example, on the Full Scale, 98 per cent of all the subjects made a gain or equalled their former IQ scores. When the scores are expressed in scale score units, only 88 per cent did so. It is also interesting to note that 92 per cent of the oldest age group showed gains and a further 8 per cent equalled their IQ scores on the Full Scale. Percentages almost as high were shown by the oldest group on the Verbal and Performance Scales.

Long-term age trends

Figure 1 shows the relationship between age and scores on the Full Scale, Verbal, and Performance Scales for the entire age range, 15 to 69 years. It can be seen that the scores on the Full Scale hold up well between the ages of 20 and 45 but decline thereafter. The slightly higher scores of the youngest subjects are not significantly different from those at ages 30 to 35, nor are those of the 40's significantly below those of the 30's ($t = 1.50$, $p > .05$; $t = 0.66$, $p > .05$). The scores of those in the 50's are significantly lower than those of the 40's ($t = 2.48$, $p > .02 < .05$). Over the range of 20 to 56, the decrease in scores is highly significant ($t = 5.12$, $p < .01$).

The scores on the Verbal Scale (the dotted lines in Figure 1) also hold up well between the ages of 20 and 45 years. None of the differences are statistically significant. However, the performance of the over-50 age group is significantly lower than that of the preceding age group ($t = 2.53$, $p > .02 < .05$).

The scores on the Performance Scale (the dashed lines in Figure 1) show a different trend; they decline gradually from the 20's to the 50's. However, when tests of significance were applied to the differences between the groups it was found that there is a significant decrease in scores between age groups I and II ($t = 2.21$, $p > .02 < .05$) and groups III and IV ($t = 2.23$, $p > .02 < .05$) but none between groups II and III. It would appear, therefore, that scores on the Performance Scale decline from the 20's to the 30's, hold up to the 40's, and then decline in the 50's.

Figures 2 and 3 summarize graphically the relationship between age and performance on the six Verbal subtests over the age range of 20 to 56 years. Of the Verbal subtests, Vocabulary, Information, and Arithmetic show no significant change with age. Comprehension,

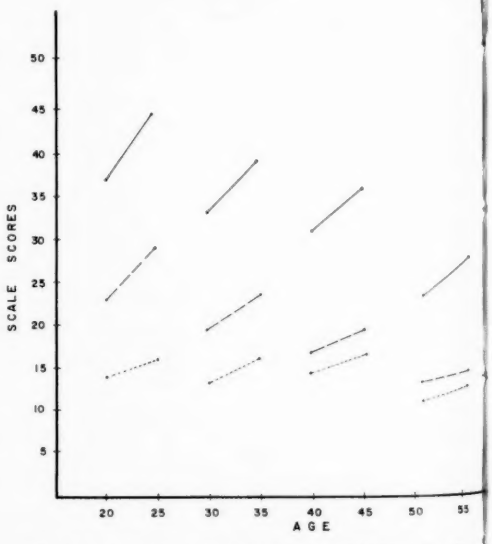

Fig. 1. Age changes in Full-Scale (continuous line), Performance Scale (dashed line), and Verbal Scale (dotted line) of the Wechsler-Bellevue.

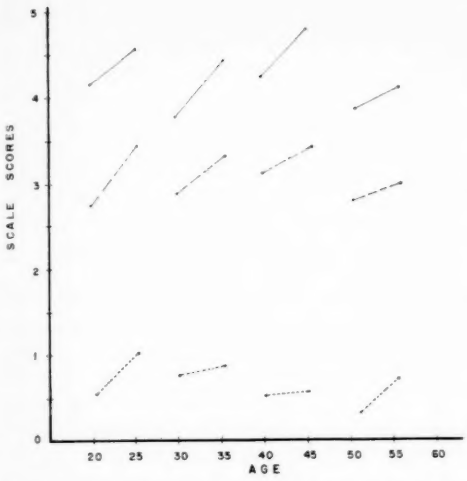

Fig. 2. Age changes on Verbal Subtests of Wechsler: Vocabulary (continuous line), Information (dashed line), and Arithmetic (dotted line).

Similarities, and Digit Span also show no significant change with age except in the 50's, where the scores on all three tests are significantly lower than in the 40's ($t = 2.52$, p = .01; $t = 2.84$, $p = .01$; $t = 2.89$, $p = .01$).

Figures 4 and 5 summarize the relationship between age and scores on the five Performance subtests. Comparison of these graphs with the preceding two shows that, in general, the Performance subtests decline earlier and more progressively than do the Verbal subtests. Figure 4 shows the relationship between age and performance on the Picture Completion and Block Design tests. In both cases there is no significant change in scores between the 20-25 and 30-35 age groups. However, on both tests there is a significant decrease in scores between 30-35 years and 40-45 years ($t = 2.23$, $p > .02 < .05$; $t = 2.15$, $p > .02 < .05$). Thus it would appear that performance on those two tests holds up to the mid-thirties and declines thereafter.

Figure 5 shows the effect of age on the scores obtained on the remaining three Performance subtests. Picture Arrangement holds up well with age, showing a significant decrease in scores in only the 50's as compared with the 40's ($t = 2.51$, $p = 0.2$). Digit Symbol shows a significant decline in the scores in the 30's ($t = 5.50$, $p = .01$) and maintains a plateau till the 50's when a significant decline is shown ($t = 3.50$, $p = .01$). Performance on the Object Assembly test is different from all other tests, both Verbal and Performance, in that it

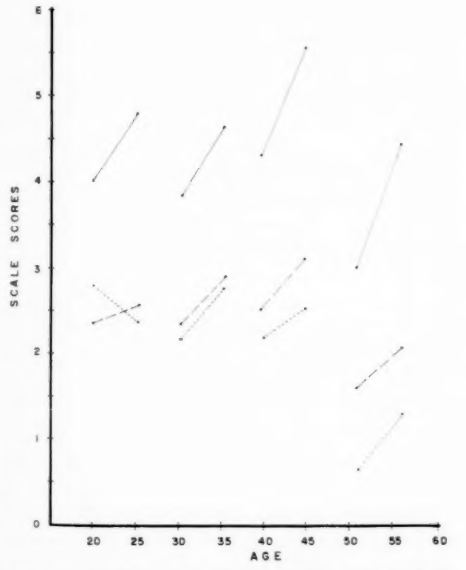

Fig. 3. Age changes on Verbal Subtests of Wechsler: Comprehension (continuous line), Similarities (dashed line), and Digit Span (dotted line).

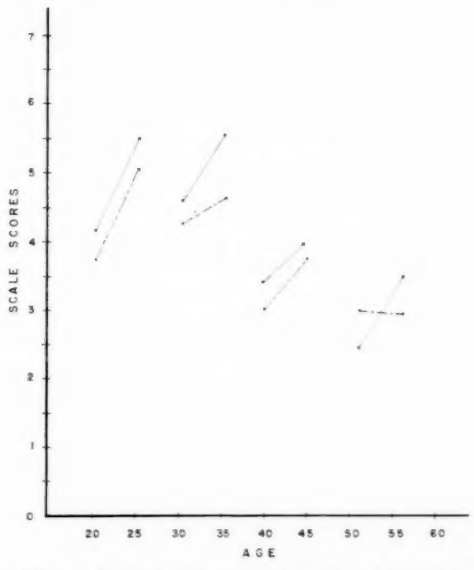

Fig. 4. Age changes on Performance Subtests of Wechsler: Picture Completion (continuous line) and Block Design (dashed line).

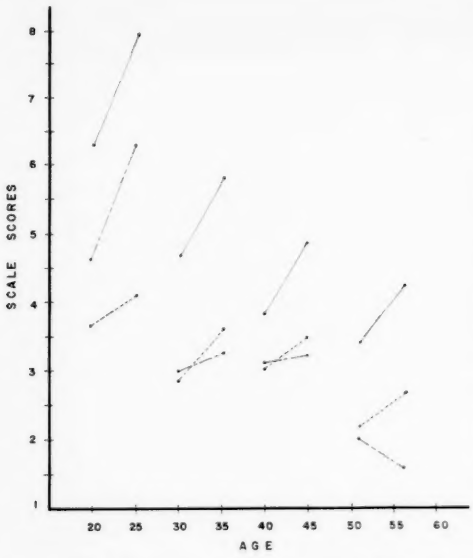

Fig. 5. Age changes on Performance Subtests of Wechsler: Object Assembly (continuous line), Digit Symbol (dashed line), and Picture Arrangement (dotted line).

falls off in the 30's as compared with the 20's ($t = 2.58$, $p = .02$), showing no further significant decline subsequently.

DISCUSSION

One of the most important findings of the present study was the demonstration that a significant improvement in intellectual performance of mental defectives could occur over a period of five years, regardless of the age at which the subjects were first tested. This increase in retest performance is found regardless of whether the results are reported in IQ scores or in scale scores. Furthermore, these significant gains are shown, not only on the Full Scale, but also on both the Verbal and Performance Scales, indicating that the improvement is quite general.

These noticeable gains in Wechsler IQ are supported by the findings of two studies carried out by Clarke and Clarke (1954) and Clarke and Reiman (1958). These investigators, retesting a group of 34 institutionalized mental defectives over a period of six years with the Wechsler Scale, also reported some surprisingly large gains in IQ. The magnitude of the gain was related to the degree of adverseness of the subjects' early environmental upbringing. Unfortunately, however, the Clarkes employed only young subjects (mean age, 25 years) in contrast to the present study where both young and old subjects were used. Nevertheless, certain significant comparisons can be made between our youngest subjects (20-25 years) and those of the Clarkes. As far as range of gain in IQ is concerned, the young subjects of the present study and the entire sample of the Clarkes showed an identical range, 3 to 22 IQ points. The correspondence is also excellent in terms of mean IQ gain when a comparison is made with those of Clarkes' subjects who came from a less adverse environment. For these subjects the Clarkes reported a mean gain of 10.2 IQ points over a six-year period. In the present study the mean gain was 9.1 IQ points over a five-year period. As far as the subjects coming from a very adverse early environment are concerned, the Clarkes reported a much larger mean gain, 16.2 points. In regard to this question of type of early upbringing, it should be mentioned again that very few of the subjects of the present study could be said to have come from a *very* adverse early environment. Thus it would appear that our findings and those of the Clarkes are essentially in agreement. Although the subjects used by the Clarkes were, on the average, quite young, some older subjects (in their 30's) were also used. These subjects also showed gains in IQ, but the gains were not as large as those of the younger ones. This finding is in keeping with the present results where gains were found at all ages but the amount of gain decreased with age. These results lend support to the Clarkes' statement that moderate gains may be made by the defective over a long period of institutional life. In the present case, however, some of the gains were quite large—e.g., 15 IQ points—after 15 or 20 years of institutional life.

Apart from the recent work of the Clarkes, no other studies using a population of mental defectives of different ages and retesting them over a period of years on the Wechsler have been carried out. Three investigations, however, have been performed using both children and older subjects in which the Stanford-Binet was employed rather than the Wechsler. The results of these studies, surprisingly, are at variance with those which have just been described. The most comprehensive of these studies was carried out by Sloan and Harman (1947) who performed 2,267 tests and retests on approxi-

mately 1500 mental defectives whose mean age was approximately 15 years—a decade younger than the youngest group in the present study. The tests-retests were over varying periods of time with the median interval between tests being 5.5 years. When a comparison of the two studies is made, it is found that 95 per cent of our entire sample showed a gain in IQ and only 2 per cent showed a loss. This contrasts with 31 per cent of the Sloan and Harman subjects showing a gain and 61 per cent showing a loss. Furthermore, this difference is still striking even when our results are expressed in scale score units. In this case, 88 per cent of our subjects gain or equal their former scores on the retest. What makes the discrepancy even more pronounced is the fact that the mean age of our entire sample is approximately 40 years, while for the Sloan and Harman study it is only 14.8 years. Our findings are, however, well in line with those of the Clarkes, who, also using the Wechsler, find 53 per cent of their subjects (mean age, 25 years) gaining more than 10 IQ points, and 26 per cent gaining more than 15 points over a six-year interval.

The second relevant investigation, also employing the Stanford-Binet, was carried out by Psyche Cattell (1931) on a group of older children of below normal intelligence. She reported an average decrease of 3.4 points over a period of from 3 to 6 years in children ranging in IQ from 70 to 89, and a decrease of 7 points for those with IQs under 69. The third study was performed by Kaplan (1943) who retested a group of 66 older morons (mean age 14 years) over a period of 15 years. Over this interval of time, he reported an average decline of 6.65 mental age months on the Stanford-Binet. Only 14 per cent of his group increased their scores. This contrasts with 64 per cent of our oldest subjects (50-55 years) who bettered their initial scores (scale score units) and another 16 per cent who equalled them.

Thus is would appear that studies using the Wechsler on a test-retest basis report consistent gains in IQ in mental defectives while studies employing the Stanford-Binet quite consistently report a loss in IQ. These apparently divergent results are undoubtedly largely due to differences in the nature of these two tests of intelligence and what they are purporting to measure. The Wechsler measures both performance as well as verbal skills, while the Stanford-Binet is largely a verbal scale. Sampling differences in the various studies are undoubtedly another important variable.

Although the test-retest studies mentioned above (using the Binet) show a consistent decrease in IQ, there are other investigations on mental defectives which report quite sizeable IQ gains on the Stanford-Binet over a period of years (Kephart, 1939; Schmidt, 1946). These latter studies are, however, in a special category since they have employed special training procedures, and gains in IQ might therefore be expected. In the present investigation no such training procedures were employed.

The problem arises, now, of accounting for the sizeable IQ and scale score gains which were made by all the age groups in the present study, including those over the age of 50 years. This question is particularly important because the consensus of opinion is that mental defectives reach their peak of intellectual ability very early in life (11 to 15 years), then begin to decline soon after (Doll, 1920; Kuhlmann, 1921; Sloan & Harman, 1947). The first variable to be considered that could account for these consistent gains is test practice. This would be a possible factor if we were dealing with subjects of average intelligence, but it is difficult to believe that it could be a significant factor in mental defectives, especially after a period of five years. Furthermore, there is evidence in the literature that test practice, unless allied with coaching, does not bring about such gains as are reported (Vernon, 1954). Finally, none of the subjects received any additional Wechsler testing at any time during the five-year period, and only a very few had been given any other type of psychological test. They were not, therefore, test oriented.

The second possible factor is the manner of administering the tests and the attitudes of the psychometrician. As far as test administration is concerned, no departures from regulation testing procedures were permitted and Wechsler's criteria for valid responses were adhered to in all tests. In regard to the attitudes and motivations of the psychometricians, none of the three testers were aware that a test-retest study was under way. There was, therefore, little likelihood that their scoring was systematically biased. A very careful analysis of the results showed that all of the testers were consistent and showed no significant differences in the scoring of answers.

A third factor which might account for the consistent gains over the five-year period is a

general improvement in the atmosphere and custodial care provided by the institution during the interval between test and retest. To our knowledge, no major change in administration or any changes in treatment or custodial care of the patients occurred during the period of the investigation.

The fourth and perhaps one of the most important variables which should be mentioned is the problem of faulty diagnosis of mental deficiency. There has been a great deal of concern expressed in the literature over this matter, especially in regard to the concept of pseudofeeblemindedness. In the minds of many researchers (Lurie, 1946; Neuer, 1947), this is a condition resembling the mental deficiency of the true "irremediable" category (Cutts, 1957; Doll, 1920), but is not of a totally irreversible nature. It is generally agreed that physical defects of speech (Arthur, 1947) and hearing (Hardy, 1949), motor deficiencies and neurotic and psychotic states (Kanner, 1949) may bring about a condition of mental functioning which well accords with the psychometric and social criteria of true mental deficiency. It is difficult to say to what degree, if any, this factor of faulty diagnosis has operated in the present study. All that can be said, however, is that the patients at the time they were admitted displayed the symptoms of true mental deficiency in terms of both psychometric ratings and social inefficiency. They also displayed these symptoms at the time they were selected for the investigation.

Recognizing the fact that physical, environmental and emotional factors may have placed limits on the growth of the mental capacities with which nature has endowed the mental defective, it is the investigators' belief that at least one of the factors responsible for the gain in IQ is the fact that these subjects were moved to the Manitoba School. The move has probably hastened the delayed maturational processes in these persons by providing them with more favorable conditions for their intellectual development. Most of the subjects of this study came from homes which could be said to have provided a relatively adverse environment, one that undoubtedly had a depressing effect upon their intellectual potentialities. Only a prolonged period of stimulation could probably counteract this effect. In this connection it has been the policy of the Manitoba School for many years to provide the best physical care, and to build an atmosphere which minimizes the custodial aspects of institutional life and accents the possibilities of rehabilitation. Especially noticeable and especially therapeutic, one would surmise, is the acceptance of the patients by the staff as worthwhile individuals. The apathy and listlessness spoken of by Goldfarb (1955) as characterizing mental defectives in many institutions was certainly not shown by the subjects of this investigation. It may be that the environment of the Manitoba School is a much more stimulating one than that existing in most other institutions for mental defectives.

This interpretation of the noticeable gains in IQ is in line with that proposed by the Clarkes (1954, 1958), who interpreted their gains, both in the young subjects as well as the older ones, as products of accelerated maturational processes occurring in a more stimulating environment. Although this explanation might account for the large gains made by our patients, who had been in the institution for five or even ten years, it is difficult to believe that the same explanation could account for the very high percentage of gains which occurred in the oldest age group, many of whom had been in the same institutional environment for 15 or 20 years or longer. One would expect that the depressing effects of even a prolonged period of exposure to an adverse early home environment would have been corrected in a much shorter interval of time.

Another way in which these results could be interpreted is to assume that the maturational processes of familial defectives show a much slower but a much longer development than those of normal persons—and possibly show a very gradual development even into the fifties. This viewpoint receives some confirmation from the study of Eustis (1947), who postulates a physiological basis for a slower maturation rate in the mental defective, viz., a much slower myelinization of nerve tracts. The Clarkes also believe that the maturation processes of defectives have a slower rate of development than those of normals. If these beliefs should prove to be true, then the slower rate of maturational development, together with living in a more stimulating institutional environment, could account for the intellectual gains shown by defectives regardless of the age at which they were retested.

Long-term age trends

It was found that general intelligence as measured by Full-Scale (scale scores) shows little if any decline from the twenties to the forties, but declines significantly thereafter. The effect of age on the scores was different on the two sections of the Wechsler. On the Verbal Scale there was no decline between the 20's and the 40's, with a significant decline occurring in the 50's. On the Performance Scale the scores declined from the 20's to the 30's, held up to the 40's, and declined again in the 50's. Since no other investigator has administered the entire Wechsler Scale to mental defectives over a wide age range, we are unable to make any direct comparison of our results with those of others. However, we can compare our results with those of subjects of average intelligence as reported by Wechsler (1944). In regard to performance on the Full Scale, Wechsler reports that a peak occurs somewhere in the mid-twenties and then the scale scores slowly and progressively decline with increasing age. In the case of our mental defectives there is little if any such decline prior to the 40's, after which the decline is somewhat steeper than for Wechsler's normals. The Verbal scores of both normals and mental defectives hold up much better with age than do their Performance scores. Certain differences appear, however, in the two groups. In the case of normal subjects, Performance scores contribute slightly more to the Full-Scale totals up to the late 20's, after which the Verbal scores contribute much more heavily. In the case of our mental defective population, the Performance scores contribute much more heavily to the Full-Scale totals at the lower age levels, with the difference gradually diminishing with increasing age. In the oldest defective group the contributions of the Verbal and Peformance scores are much more equal, 11 points difference in the 20's having decreased to less than two points in the 40's. This differential pattern of performance has been assumed by several investigators (Halstead, 1943; Rabin & Guertin, 1951) to be typical of the subtest performance of the mental defective.

An analysis of the scores obtained on the six tests making up the Verbal Scale and the five tests making up the Performance Scale showed a differential pattern of age changes. The most relevant study with which to compare our findings was carried out by Thompson (1951), who administered to a group of 137 defectives varying in age from 16 to 69 years a number of tests taken from the Wechsler, viz., Picture Arrangement, Digit Symbol, Block Design, Vocabulary, and Digit Span. For the two Verbal tests, Vocabulary and Digit Span, he reported no decrement whatever between the ages of 16 and 69. This is in line with our results on Vocabulary and also on Digit Span (with exception of those in their 50's who showed a significant decline). On the three Performance tests, Thompson reported significant losses at age 30, as compared with age 20, after which the only significant decrease was from 40 to 50 years in Digit Symbol. Our results are in agreement with his on Digit Symbol. However, for Picture Arrangement our results show no significant decrease until the 50's are reached. Block Design also shows a later falling-off than that found by Thompson, for the initial decrease is found when the scores of the 40's are compared with those of the 30's, with no further decline being noted.

The discrepancies between our and Thompson's results are very likely due to two factors, differences in the nature of the samples used, and a difference in approach. Thompson restricted his subjects to an IQ range of 50 to 70, while in the present study the range of IQs was much wider. Also, in the present study more older subjects were used than in Thompson's. Thompson employed a strictly cross-sectional approach, while in the present investigation a combined longitudinal (test-retest) and cross-sectional approach was employed. There are some suggestions in the literature that different aging results may be obtained depending upon whether a longitudinal or cross-sectional approach is used (Goodenough & Tyler, 1959).

Again to compare our mental defectives with normal subjects, Wechsler (1944), in examining the effects of aging, divided the subtests of his scale into two groups which have become widely known as the "hold" and "don't hold" tests. Along with three Verbal tests in the "hold" category, Information, Comprehension and Vocabulary, he has included two Performance tests, Object Assembly and Picture Completion. Other investigators (Berkowitz, 1953; Hunt, 1949; Madonick & Solomon, 1947) agree that these three Verbal tests hold up with age, but disagree regarding the two Performance tests, maintaining that these two really belong in the "don't hold" category (Hunt, 1949; Rabin & Guertin, 1951). The present

study is in agreement with Wechsler that the three Verbal tests hold up very well with age. There is some disagreement on the two Performance tests, where Picture Completion in mental defectives holds up well only into the 30's, and Object Assembly begins to decline after the 20's.

In the "don't hold" category, Wechsler has included the remaining three Verbal tests, Arithmetic, Digit Span and Similarities, and the remaining Performance tests, Block Design, Digit Symbol and Picture Arrangement. On these tests our results on mental defectives are at considerable variance with Wechsler's on normal subjects. Only on Block Design and Digit Symbol is there a noticeable falling-off in performance with age, while the three Verbal tests and Picture Arrangement hold up well. The findings of this study follow much more closely those of Rabin and Guertin (1951), who placed all the Verbal subtests in the "hold" category and the Performance subtests in the "don't hold." They also conform much more closely to Hunt's (1949) work on "hold and don't hold" tests on normals. On the whole it would appear that the subtest performance with age of both mental defectives and normals is quite similar.

A final question arises from the apparent discrepancy in these results in which intellectual gains were obtained in all age groups on a test-retest basis but some losses occurred when the results were plotted over the entire span of years. It is the investigators' belief that this discrepancy is in large measure due to the methods used. In the first case the longitudinal method was used where the same subjects were tested over a period of five years. In the second case this method together with a cross-sectional one was used where the subjects were of different ages at the time the study was begun. In studies using the longitudinal method it has almost invariably been reported that intellectual abilities hold up or improve with age (Bayley & Oden, 1955; Owens, 1953). In studies employing the cross-sectional method a decline has almost invariably been reported (Jones & Conrad, 1933; Wechsler, 1944). Although these investigations employed subjects of average or above average intelligence, it is quite likely that the same situation may apply to the mental defective population. The longitudinal approach provides a more accurate and valid picture of age changes, for the same individuals are being studied and consequently the sampling problem is not too important. On the other hand, the cross-sectional approach presents some almost insurmountable sampling problems, especially when older age groups are involved. These sampling problems are especially difficult in the case of institutionalized mental defectives. In this case the older defectives are usually those of lower intellectual capacity (or of poor social adjustment) who have failed to reach the standard necessary for rehabilitation.

SUMMARY

One hundred familial mental defective patients were divided equally into four groups with mean ages of approximately 20, 30, 40, and 50 years. They were all given the Wechsler-Bellevue Intelligence Scale and then were retested five years later on the same test. Significant mean gains were found in all four age groups on the Full, Verbal, and Performance Scales, gains which were shown in the scale scores as well as in IQ units. Full Scale and Performance Scale gains diminished with age, while larger Verbal Scale gains were shown at the older age levels. Ninety-eight per cent of the subjects either increased or equalled their former IQ scores.

Over the entire age range studied, scale scores on the Full Scale held up well between the ages of 20 and 45, but showed a decline thereafter. Verbal scale scores showed no appreciable decline until the fifties. Performance scale scores declined gradually from the 20's to the 50's. The apparent discrepancy between the consistent gains obtained on all of the retests and the slight decline appearing when the scores are plotted over the entire age period was attributed largely to differences between longitudinal and cross-sectional methods.

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DIFFERENCES BETWEEN OLD AND YOUNG EXECUTIVES ON OBJECTIVE PSYCHOLOGICAL TEST VARIABLES

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As part of a larger program[1] designed to predict successful executives, data were collected for two groups of executives: the first consisted of 150 men aged 35 and under at the time of testing; the second consisted of 150 men aged 45 and over. (The mean age for the younger group was 31.2, with a range from 21 to 35 and a standard deviation of 2.7. For the older group, the mean age was 50.4, the range was 45 to 62 and the standard deviation 4.6.) These executives were tested on 29 objective psychological test variables designed to reveal what psychological characteristics distinguish the younger from the older executive; and to promote understanding of what psychological changes, if any, might be expected with advancing age for this specific occupational group. The importance of such knowledge is reflected in labor statistics which show larger percentages of those people gainfully employed in managerial positions to be in upper age brackets: while 21 per cent of individuals between the ages of 45 and 54 are included in the "proprietors, managers, and officials" category, fully 32 per cent of those 65 and over fall into that grouping (Mering & Weniger, pp. 298-299).

POPULATION AND TEST VARIABLES

Aside from the age factor, the individuals chosen for this study were selected randomly from those executives tested and evaluated by the firm of Edward N. Hay & Associates between the calendar years 1956-1958. The younger group was composed of men whose job classifications ranged from management trainees to middle management personnel. Their average salary was $6,079 per year, with a range from $3,000 to $8,200. The older executives were all middle management and high level management personnel. Their mean salary was $12,304 per year with a range from $6,300 to $60,000. These individuals were regarded as executives because they "assign general objectives, taking into account the various forces which bear on an organization's functioning and assuming responsibility for end results." This definition seemed to parallel those suggested by other experts in the field. For example, Heffner, summarizing the various criteria used to define an executive, settled on the four primary functions of planning, organizing, directing, and controlling (Heffner, 1954).

The executives were drawn from eleven different companies. The distribution of cases in each company was mainly a function of the size of the testing program conducted on each company. The disproportion of cases per company represents a possible limitation of this study. Table 1 reports the number of executives in each age group for each company.

The psychological tests used in the study were:

1. Wechsler Adult Intelligence Scale (Total IQ).
2. Vocational Aptitude Examination, Type E-A, including 5 of 8 subtests: General Information; Arithmetic Reasoning; Judgment in Estimating; Reading Comprehension; and Vocabulary.
3. Kuder Preference Record, Personal, Form A.
4. Kuder Preference Record, Vocational, Form B.
5. Guilford-Zimmerman Temperament Survey.

Altogether, these tests included 29 variables of intelligence, interests and temperament. Since the tests used in this study are well known, a detailed description of the 29 variables will not be given here. The reader is referred to the respective test manuals for additional information.

RESULTS

Means and standard deviations were computed for the younger and older groups respectively on the 29 test variables. Two-tailed tests of significance for differences between the means of each group on the 29 variables, and *F* ratios for significance of differences between the standard deviations were also computed. Table 2 reports these results.

[1] This program was conducted under the auspices of Edward N. Hay & Ass., Inc., management consultants, Philadelphia, Pa.

At the .01 level of confidence the older executive as compared to the younger executive was less interested in being active in groups, working with ideas, directing others and persuading others. He had a greater preference for mechanical and artistic pursuits. On the Guilford-Zimmerman Temperament Survey the older executive scored lower on Ascendance, Sociability, Emotional Stability, and Objectivity. At the .05 level of confidence the older executive was more interested in familiar and stable situations and in scientific endeavors, and scored higher on the restraint category of the Guilford-Zimmerman. In short, in terms of interests and temperament, the younger executive scored higher on those variables which might *a priori* be associated with the typical executive.

At the .05 level of confidence the older executive scored higher on the WAIS but lower on the Reading Comprehension section of the VAE.

Comparison of the variability of the two age groups reveals seven significant differences between the standard deviations, all of these differences showing larger variability in the older age group. At the .05 level the older group displayed greater variability in emotional stability. At the .01 level of confidence the older group was more variable in: VAE—General Information, Reading Comprehension, and Vocabulary; KPRV—Directing Others; and GZ—Ascendance and General Activity.

DISCUSSION

As a precautionary note it should be remembered that the older executive may represent an even more select group than the younger executive, the forces of competitive attrition having eliminated the less able individual from the executive ranks with the passage of time. Nonetheless, it is interesting to note that intellectual abilities hold up comparatively well with advancing age for this executive group. This is in accordance with other studies which show that upper intelligence groups may be expected to retain their comparative superiority with increasing age (Anastasi & Foley, 1949, p. 286; Bayley & Oden, 1955). Also, more recent studies with the WAIS seem to indicate that intellectual ability does not deteriorate as rapidly with age as was previously anticipated (Anastasi, 1956, p. 509).

Unfortunately, mean raw scores (instead of

TABLE 1. NUMBER OF EXECUTIVES IN EACH AGE GROUP.

Type of company	Number of cases	
	Age 45 and over	Age 35 and under
Aviation (A)	4	0
Insurance (A)	4	0
Manufacturing (A)	0	10
Manufacturing (B)	0	1
Utility	67	50
Insurance (B)	19	21
Manufacturing (C)	6	0
Chemicals	4	0
Insurance (C)	32	68
Engineering	13	0
Aviation (B)	1	0
Total	150	150

TABLE 2. MEANS AND STANDARD DEVIATIONS FOR THE YOUNGER AND OLDER EXECUTIVE GROUPS ON 29 PSYCHOLOGICAL TEST VARIABLES.

Variable	Means		Standard Deviations	
	Younger	Older	Younger	Older
Wechsler Adult Intelligence Scale	122.0	124.6*	10.0	10.3
Vocational Aptitude Examination:				
General Information	32.3	32.8	5.6	7.7**
Arithmetic Reasoning	9.4	9.0	4.0	4.2
Judgment in Estimating	53.9	56.2	13.3	14.5
Reading Comprehension	14.7	13.5*	4.0	5.0**
Vocabulary	17.0	17.6	6.3	9.5**
Kuder Preference Record, Personal:				
Active in Groups	77.9	61.6**	23.1	25.9
Familiar and Stable Sit.	38.4	46.2*	25.2	28.2
Working with Ideas	60.2	49.9**	28.2	27.0
Avoiding Conflict	54.4	53.5	28.6	27.9
Directing Others	80.8	63.7**	19.4	26.5**
Kuder Preference Record, Vocational:				
Mechanical	38.6	49.3**	24.5	26.7
Computational	52.9	51.7	31.5	28.2
Scientific	39.8	47.0*	28.1	26.1
Persuasive	63.3	46.9**	28.6	28.3
Artistic	41.3	49.5**	30.5	28.4
Literary	58.2	52.3	29.5	30.8
Musical	55.4	50.0	27.0	26.7
Social Service	54.7	50.3	26.1	29.3
Clerical	48.1	46.1	28.5	26.5
Guilford-Zimmerman Temperament Survey:				
General Activity	18.5	17.1	5.4	7.4**
Restraint	19.1	20.1*	4.4	3.9
Ascendance	19.3	16.5**	5.3	6.9**
Sociability	22.4	19.0**	5.5	6.3
Emotional Stability	21.9	19.8**	4.5	5.5*
Objectivity	21.6	19.8**	4.5	4.8
Friendliness	17.7	17.2	4.5	5.0
Thoughtfulness	18.5	19.3	4.4	4.6
Personal Relations	23.0	22.8	4.2	4.2

* Difference reliable at the .05 level of confidence.
** Difference reliable at the .01 level of confidence.

age-corrected scale scores for total IQ) which would have made possible a more meaningful comparison of absolute intellectual ability, were not available. WAIS subtest scores were also unavailable, so that analysis of the differential effects of age on intelligence had to be restricted to the VAE scores. All subtests on the VAE are timed, and place some emphasis on the speed factor. Traditionally, the older person is supposedly placed at a disadvantage on speeded intelligence tests items (Anastasi & Foley, 1949, p. 288), although more recent studies seem to indicate that time limitations are not as important as was previously thought (Schaie, Rosenthal, & Perlman, 1953; Wechsler, 1955, p. 277). Whether due to the special attributes of the older executive, or to the general inconsequence of time limits in measuring intellectual level of older people, the older executives compared favorably to the younger executives on the speeded VAE subtests. The younger group held a slight but significant edge on only one subtest, VAE Reading Comprehension. It must be concluded, then, that differences in intellectual ability between older and younger executives, even when significant, are comparatively small.

In contrast to the relatively small differences in intelligence test performance, significant disparities are evident along the interest and temperament variables. These disparities not only parallel other findings in the field, but also suggest a definite pattern of withdrawal and retrenchment in older aged executives. Studies on interest changes with age show decreased preferences for dangerous activities, varied pursuits, and social contacts (Pressey & Kuhlen, 1957, p. 394; Strong, 1934; Strong, 1943). Kelly (1955) noted a loss of self-esteem, and Cattell (1957), interpreting Kelly's findings within his own factorial scheme, reported drops in Radicalism, Surgency, and Id Pressure with increasing age. These studies must be interpreted with caution since they do not deal specifically with executive groups. However, a projective study by Schaw and Henry (1956), with a sample of 45 urban, American business executives, lends credence to these past findings. Schaw and Henry used samples which, while restricted in number, closely approximated the groups reported in this present study: a "young" group with a mean age of 30.5, and an "old" group with a mean age of 50.6. Based on dominant TAT thema, the study indicates (as attributes of the older group) less optimism, less reliance on inner resources as a means for problem solving, a proclivity for sacrificing inner needs when they conflict with achievement, and a tendency toward perceiving problem situations as complex and sometimes unsolvable. By integrating previous findings with those of the present study, a pattern of conservatism, pessimism, lessened energy and withdrawal seems to emerge for the older aged executives.

As an alternative, more optimistic hypothesis, the differences in interests might be explicable in terms of broadened interests resulting from a lessened concern with advancement. The older executive, being more securely ensconced in the managerial heirarchy, may have a greater affinity for familiar and stable situations. Having less need to prove himself, he may not need to display high interest in being active in groups, working with ideas, directing others, and persuading others. Also, with security may come broadened interest in science, art, and mechanical areas. Increased restraint and lower scores on ascendence, sociability, emotional stability, and objectivity as measured by the Guilford-Zimmerman may reflect a more confident, secure, and honest appraisal of oneself, unhampered by deliberate or unconscious attempts to manifest those traits traditionally associated with a successful executive.

Whether these significant differences in interest and temperament are artifacts of a more relaxed and honest testing attitude, or whether they reflect important changes with age is a problem for further research, although the evidence seems to favor the latter assumption.

The finding that variability is greater in the older age group agrees with the summarization by Anastasi and Foley that "variability tended to increase with age, despite the decline in average scores." While this statement is based on intelligence test measurements the same may be true of interest and temperament, since "It would seem that, as the individual's experiential background is enriched with age, more sources of variation are introduced and individual differences continue to increase" (Anastasi & Foley, pp. 284, 285).

Variability increases with age have also been noted in psychomotor performance (Miles, 1931). Whether increased variability is due to enriched life experiences or to some other more specific factor such as differential rate of biological and psychological aging is a matter for conjecture. At any rate, this study provides further substantiation for past findings indicating increasing test variability with age.

SUMMARY

A younger and an older group of executives were compared on 29 objective test variables covering intelligence, interest, and temperament. Differences in intelligence were negligible. Larger differences were noted in interest and temperament and may reflect general personality changes relative to aging. There were also significant differences in variability between the two groups, with the greater variability shown in the older age group.

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CHANGING PATTERNS OF RETIREMENT*

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Among the meaningful activities in which elderly persons might engage, work for pay or profit is declining in relative importance. In 1900, out of a population of slightly more than three million persons aged 65 and over, approximately two out of five were gainful workers. By 1959, the population in this age group had expanded to nearly 15 million, of whom only about one in five was in the labor force. Thus, as the number of elderly persons in the population has increased, the number of nonworkers has risen much more rapidly than the number of workers.

The demographic changes that are responsible for the marked increase in the number of older people in the population are by now thoroughly familiar. There is also general awareness of the fact that the decline in the percentage of workers in the aged population is entirely attributable to a fall in the proportion of elderly men in the labor force. The percentage of elderly women in the labor force has been very small throughout the present century but has risen slightly in recent years.

The striking increase in the number of nonworkers in the aged population, with its parallels in all industrialized nations, has been responsible for a marked upsurge of interest in the issue of work versus retirement for elderly people. Much of the discussion of this issue has revolved around the question of compulsory versus flexible retirement policies. This is part of the problem, and a growing part, but there are many other aspects of the issue of work versus retirement for elderly people that require study and debate.

In a broader sense, the issue of work versus retirement for older persons involves all those aspects of management, union, and government policy that affect the decisions of older persons to work or retire. Policies affecting the hiring and retention of the older worker, the adequacy of public and private pension benefits, the availability of disability and health insurance, the retirement age and retirement test under the Social Security Act, and retirement programs for government employees are all closely related to the problem. And in a less direct but even more important sense, all those aspects of social policy that affect the general level of employment are highly relevant.

If intelligent decisions are to be made on these questions, a great deal of information bearing on the circumstances and conditions under which people actually retire is needed. There has been a substantial amount of research on attitudes toward work and retirement, chiefly among the employees or retirees of sizable corporations, and some significant research on reasons for retirement. But there has been surprisingly little study of the actual process of retirement as it is experienced by large groups of elderly persons who have not been employed by large corporations. Even so, it is possible to piece together a somewhat impressionistic picture of various patterns of retirement on the basis of scattered sources of information, and to draw certain inferences that are highly relevant to issues of retirement policy.

THE LIFE CYCLE IN WORK PATTERNS

By no means do all persons work steadily to age 65 and then abruptly retire. An understanding of patterns of retirement requires, first of all, an accurate picture of the life cycle in patterns of work. The proportion of men in the labor force rises to a peak at ages 35 to 44 and then declines steadily with advancing age. However, the decline is quite gradual up to about age 55 and then begins to accelerate. At ages 65 to 69, only about half of all men are in the labor force, while among men aged 70 and over approximately a fourth are working or seeking work.

Equally significant is the fact that among the men who work, middle-aged men are more likely to work full time the year round than

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either younger or older men. The older male population includes not only a large percentage of men who have left the labor force, but also a substantial proportion who are working part time or intermittently. Among those aged 65 and over who are in the labor force, only about four out of ten work at full-time jobs the year round.

The life cycle in labor force participation of women has undergone a striking change since 1900. Whereas formerly the proportion of women in the labor force reached a peak in the age group from 20 to 24 and then descended sharply, it now rises to a second peak at ages 45 to 54. If recent trends continue, this second peak is likely before long to be substantially higher than the peak in the early twenties. However, the proportion of women aged 65 and over in the labor force is very small, amounting only to about 10 per cent.

Full-time work plays a relatively less important role in the lives of female workers of all ages than in the case of men, and among women aged 65 and over full-time work is rare indeed. Even within the relatively small group of these elderly women in the labor force, less than a third work full time the year round. Most of the others work on a part-time basis.

THE PROBLEM OF RETIREMENT

If patterns of work vary greatly with changing age, so do attitudes toward retirement. For the young man who is primarily concerned with his current and future job status, retirement is a distant prospect. But increasing age tends to be accompanied by increasing apprehension over the prospect of retirement. Indeed, there are indications that, the closer the worker comes to retirement age, the more likely he is to repress the whole idea (Crook & Heinstein, 1958). And there is growing evidence that once this critical stage is behind him and he is actually retired, his attitude may become less negative (Thompson, 1956).

Attitudes toward retirement also differ greatly among occupation groups. Friedmann and Havighurst (1954) found that the proportions of men who wanted to continue working fell sharply between the top and the bottom of the occupational scale. However, the Cornell retirement study (Thompson & Streib, 1958) suggests that, except for professional workers, persons at higher occupational levels tend to look more favorably on retirement than those in the lower occupation groups. The study also indicates that the more favorable attitudes of workers in the high occupation groups appear to be closely associated with the fact that they can look forward to a higher retirement income.

Although professional and managerial workers are particularly likely to find their work intrinsically interesting, they likewise have a greater tendency to make careful preparations for retirement and are more likely to have in mind a number of leisure-time activities which they expect to enjoy in retirement (Burgess, Corey, Pineo, & Thornbury, 1958). As one writer has put it, the whole idea of planning for retirement may well be a middle-class concept (Barron, 1956).

Contrary to a widespread impression, involuntary retirement provisions are not the most prevalent reason for retirement, except perhaps in relatively large corporations. Several nationwide studies conducted in the early 1950's indicated that only a small proportion of retired workers had been forced to retire because of involuntary retirement provisions. Most of the retired workers had quit their jobs voluntarily, and in the great majority of these cases failing physical capacity and ill health were the reasons cited for quitting (Friedmann & Havighurst, 1954; Stecker, 1955; Steiner & Dorfman, 1957). In addition, an appreciable percentage of retired workers had left the labor force because their jobs had been discontinued, or because they had become involuntarily unemployed for other reasons.

It is likely, however, that the proportion of workers retiring because of involuntary retirement provisions is higher now than in the early 1950's, a point to be elaborated below.

PATTERNS OF RETIREMENT

It is apparent that retirement is a process which occurs in many different ways. Probably the most important patterns are: 1) retirement at the normal retirement age, or a later age, under the provisions of a formal retirement system; 2) early retirement under a formal system, sometimes followed by a shift to other employment; 3) retirement from a stable job in a firm without a formal retirement system; 4) an unstable pattern of retirement in which an older worker (a) loses a stable job and is subsequently forced to rely on unsteady or part-time employment until he finally leaves the labor force or (b) has been engaged in casual or

short-term employment and finds it increasingly difficult to get work as he grows older.

Although only a minority of workers retire under the provisions of formal retirement systems, there is ample evidence to suggest that the proportion is growing. Since few firms have formal retirement systems in the absence of a pension plan, data on the growth of pension plans may be relied on to provide an indication of the spread of formal retirement systems. The number of workers covered by private pension plans increased from 2.7 million in 1930 to 19.0 million in 1958, or from 5.4 per cent to 28.8 per cent of the civilian labor force (Holland, 1959; U. S. Social Security Administration, 1959). In addition, more than four million government employees were members of retirement systems in the latter year (U. S. Social Security Administration, 1960). Thus, nearly a third of the civilian labor force was covered by a pension plan or a government retirement system.

Pension plans are more likely to be found in large firms than in smaller companies. Coverage also varies widely by occupation and industry.

Pension experts are inclined to think that the rapid growth in pension coverage which has characterized the 1940's and 1950's is not likely to continue, and that growth will proceed at a slower rate in the years to come. As Holland (1959, p. 127) has put it, the "more likely situations for the introduction of pension plans have already been tapped, and only the harder cases remain." Yet it must be kept in mind that the most rapid gains in employment are occurring chiefly in white collar occupations and in such sections of employment as finance and government, in which pension plan coverage is comparatively high. Thus, the percentage of the civilian labor force under pension systems may continue to increase at a fairly rapid rate because of shifts in the structure of employment.

Most of the available evidence suggests that, among workers covered by pension plans, the proportion subject to some type of involuntary retirement policy is very high indeed. However, involuntary retirement provisions are somewhat less prevalent under negotiated pension plans than under unilateral plans. The relatively rapid growth of negotiated plans during the 1950's has apparently resulted in a slight decline in the relative importance of involuntary retirement provisions, and in some tendency to stipulate age 68 or 70, rather than age 65, as the required retirement age where involuntary retirement prevails. Age 65 continues, however, to be the involuntary retirement age in the great majority of unilateral plans (Bankers Trust Company, 1956). Nevertheless, since the proportion of workers covered by pension plans has been increasing rapidly, the percentage of all workers affected by involuntary retirement provisions has undoubtedly been rising substantially, despite a slight decline in the proportion of pension plans with involuntary retirement provisions.

Just recently, as a result of the sluggishness of the recovery of employment in the wake of the 1957-58 recession, there have been indications of a rise of sentiment within union circles, reminiscent of the 1930's, in favor of involuntary retirement, or of lowering the retirement age in order to get older workers off the labor market and improve job opportunities for younger workers.

Only scanty data are available on the percentage of workers who retire with pension benefits before the normal retirement age, but such studies as have been made on the age of retirement from private employment suggest that the proportion may be as high as 20 to 30 per cent (Life Extension Foundation, 1956). However, little is known about the extent to which these workers later take other types of jobs. Under retirement plans for federal government employees, early retirement is much more prevalent than in private industry, approximating 60 per cent of all annuitants under the civil service retirement system (Committee on Retirement Policy for Federal Personnel, 1954).

Probably the most typical pattern of retirement is from a steady job in a firm without a pension plan. Ill health is clearly the most prevalent reason for retirement for this group, and inadequacy of retirement income tends to be a critical problem. Only those relatively few who have received comparatively high incomes are likely to have accumulated enough savings to provide any appreciable supplement to social security benefits. And despite the succession of increases in OASDI benefit levels adopted during the 1950's, the average benefit received by a single retired worker is only about $73 a month.

This is not to suggest that workers retiring from firms with pension plans always receive adequate benefits. But the combination of a private pension and OASDI benefits is more

likely to approach adequacy than is the latter alone. Nor does the answer to the problem necessarily lie in the direction of extending private pension plan coverage to all workers not now included under such plans. An alternative approach would be a very substantial increase in the average level of OASDI benefits.

Although there is little direct information bearing on the point, a reasonable inference can be drawn from scattered data that workers retiring from firms without pension systems would, on the average, retire earlier if they could look forward to an adequate retirement income.

Unstable patterns of retirement are experienced by substantial numbers of elderly workers who undergo prolonged spells of unemployment and never again succeed in getting steady jobs. Unstable patterns are also to be expected in certain occupations (e.g., farm labor, lumber work, and building trades) in which work is typically seasonal or short-term in character. Workers in these industries are likely to find it increasingly difficult to achieve steady employment in the later years of working life.

In many respects the retirement problems of these groups resemble those of workers retiring from steady jobs without private pensions. But the personal financial assets of the former as they approach retirement are likely to be even less adequate because of the drain imposed by periods of unemployment. Further, the OASDI benefits for which they are eligible are likely to be lower because of the impact of these same spells of unemployment on their average monthly earnings under the system.

CONCLUSIONS

There is little doubt that the ratio of workers to nonworkers in the aged population will continue to diminish. But how rapidly the decline will occur in the next decade or two will depend primarily on conditions in the labor market. If the rate of expansion of employment opportunities—in a period when the supply of youthful workers will be rising sharply — is not high enough to absorb the increase in the labor force, the decline in the proportion of workers in the older population is likely to be accelerated.

Even if a satisfactory rate of employment expansion is achieved for the economy as a whole, the gains are likely to occur chiefly in white collar employment. In an age of automation and rapid technological change, expansion of employment in many blue collar sectors has come to a halt in recent years, and in a growing number of industries employment of manual workers is declining. In this type of environment, there is likely to be pressure from the younger members of a good many unions for more restrictive retirement policies to hasten the retirement of older members.

If this happens, it is to be hoped that the alternatives will be carefully weighed and examined. Apart from broad national policies designed to stimulate the expansion of employment, what is needed, above all, is a flexible approach by both management and labor to the problems of technological change and declining employment in particular industries. Examples of imaginative approaches to these problems are represented by the mechanization fund recently established for West Coast longshoremen and by the automation fund set up by the Armour Company.

In the first instance, West Coast longshoremen are referred to jobs through a union dispatching service aimed, in general, at sharing the work equitably among members of the "fully registered work force." In its 1959 agreement with the union, the Pacific Maritime Association accepted the principle that union members were entitled to a share in the savings resulting from mechanization and undertook to accumulate out of such savings a special "mechanization" fund, to be distributed among members of the fully registered work force. The basis of distribution was to be left for later determination, but it was anticipated that the fund would be used to compensate workers for reduced employment resulting from mechanization (Memorandum of Understanding, 1959).

The 1959 agreement between Armour and Company and the United Packinghouse Workers established an "automation" fund, to be administered by a special management-labor committee with an impartial chairman. The committee was to conduct special studies and make recommendations with respect to use of the fund, "including training employees to perform new and changed jobs and promoting employment opportunities within the Company for those affected" by technological changes (Master Agreement, 1959-1961, p. 116).

Even if it is agreed in some industries that the retirement of older workers should be speeded up, alternative methods of achieving this result should be carefully considered. Is it more desirable, for example, to facilitate voluntary retirement through more adequate retirement benefits or to hasten retirement through introducing or lowering a compulsory retirement age? What are the differential effects of these two alternatives on the types of workers who retire at given ages, and what are the relative costs involved if one takes into account the probability that involuntary retirement provi-

sions have a greater tendency to bring about the retirement of workers who are still highly productive?

In considering the various alternatives available, moreover, there is a need to give more thought to the implications of the increase in life expectancy. Age 65 has been selected as the compulsory retirement age under many retirement programs since the latter part of the nineteenth century. Yet life expectancy, even for those who have already reached age 65, has been gradually increasing. A major breakthrough in the battle against either heart disease or cancer could greatly accelerate this trend. Even if the rate of expansion of employment opportunities should slow down, would it be wise to consider forcing retirement at earlier ages in spite of increased life expectancy? And in those employment situations in which a compulsory retirement age is considered essential, should some thought be given to a gradual increase in the required retirement age?

If the increase in the ratio of white collar to blue collar workers is creating apprehension in union circles concerned about sluggish employment opportunities for manual workers, it also has many other important implications in relation to the retirement picture. Along with this change there is likely to be a decline in the proportion of workers retiring because of ill health, and there may also tend to be a decrease in the proportion retiring as a result of a prolonged spell of unemployment, since these reasons for retirement are relatively less important for white collar workers. But, for reasons already suggested, there is also likely to be a substantial increase in the proportion of workers retiring under the provisions of formal retirement systems. Hence the question of compulsory versus flexible retirement, although it is only one among many issues of retirement policy, is likely to be a matter of vital concern to a growing proportion of workers.

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LONGEVITY AND INTELLECTUAL VARIATION IN A SENESCENT TWIN POPULATION*

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While sufficient data are lacking on the interaction of genetic and ecological factors in regard to the capacity for survival to old age, a genetically determined relationship between parental and filial life expectancy has been demonstrated from family data as well as from twin investigations (Bell, 1918; Jalavisto, 1951; Kallmann, Aschner, & Falek, 1955; Pearl & Pearl, 1934). Furthermore, in a series of twins where both partners died of natural causes after age 60, earlier analyses showed mean intra-pair differences in life span that were consistently larger in two-egg than in one-egg twins (Kallmann, *et al.*, 1955; Kallmann & Jarvik, 1960; Kallmann & Sander, 1948; Kallmann & Sander, 1949).

Psychometric cross-sectional studies on changing intellectual functions in senescent twins yielded evidence of a consistent decline with age, beginning in the fourth decade of life (Birren & Botwinick, 1951; Doppelt & Wallace, 1955; Goldfarb, 1941; Jones & Conrad, 1933; Lorge, 1947; Wechsler, 1944). On the other hand, longitudinal investigations of changes in intellectual abilities during a comparable period prior to senescence failed to reveal an equivalent decrease (Bayley & Oden, 1955; Kaplan, 1943; Owens, 1953).

The present report on a twin-family study organized in New York State in 1945 serves a twofold purpose: 1) to present some final statistical data which have accrued during the 12-year follow-up period, and 2) to continue the evaluation of longitudinal twin data on declining intellectual functions during senescence.

The sources of ascertainment and distribution by sex and zygosity of the 1019 twin pairs formed by the 1603 senescent twin index cases are illustrated in Table 1. As previously defined (Jarvik, Falek, Kallmann, & Lorge, in press), an index case was a person 60 years of age or over, of a multiple birth, residing in or near New York State. If the 166 unclassified pairs are disregarded (most had same-sex cotwins who died at an early age), the ratio of one-egg to two-egg pairs in our sample is 261:592.

With a rate of 30.6 per cent for one-egg twin pairs, our figure falls between that obtained (Weinberg, 1902) for monozygotic twins born in the United States between 1890 and 1900 (25.6 per cent) and that found (Yerushalmy & Sheerar, 1940) for monozygotic twins born in New York State in 1936-1937 (32.6 per cent). Since these figures were based on birth statistics, no real estimate is availble for the proportions of one-egg and two-egg twins expected in the senescent age range (Allen, 1955). The representativeness of our sample is indicated by the composition of the two-egg series where same-sex and opposite-sex pairs (297:295) show the theoretically expected 1:1 ratio.

It is not surprising that the largest proportion of senescent twin pairs (61.8 per cent) has been collected from the general population. The relatively small number of cases ascertained from old age homes was probably due to the fact that institutionalized old people away from their homesteads were unable to supply reliable family histories. In the mental hospitals, where records of family data are maintained, ascertainment was virtually complete.

In 584 of 1019 twin pairs included in the study both twins qualified as index cases, while only one member of each pair met the criteria in the remaining 435 pairs. The cotwins of these 435 index cases either died before age 60 or failed to meet the residency requirements.

Longevity

The longer life span of the female expressed itself in a preponderance of female pairs in the same-sex group (420 out of 724). Further evidence for this sex difference in the human life span is provided by our series of 753 deceased index twins. The mean length of life of 348 males was approximately three years shorter

* Grateful acknowledgment is hereby made of the financial assistance received from the Rockefeller Foundation (1945-1951) and the Division of Research Grants of the National Institutes of Health (1952-1959).

than that of 405 females (891 and 930 months, respectively).

Since the data supporting the genetic theory of longevity potentials have been derived from twin subjects in this study, their general significance depends on whether or not they are applicable to the total population. More specifically, it is to be determined whether or not, after a given age has been reached, senescent twin individuals live as long as all persons. The need for such a comparison is obvious in view of the fact that during the first year of life twins are known to have a higher mortality than single-born infants, while it is assumed that twins have the same life expectancy thereafter as single-born persons (Allen, 1955). One method of investigating this point further is to compare survivorship beyond age 60 of the senescent twin population with that of a comparable white United States population. The results of such an analysis are shown in Table 2 for succeeding five-year periods. If survival rates in the general population are compared with those of the eight sex and zygosity groups of our twin population, it can be seen that the life expectancies of the two populations are of the same order of magnitude.

A summary of our final data on the observed mean intra-pair differences in life spans between senescent twin partners, where both died of verified natural causes at age 60 or over, is given in Table 3. After 12 years of observation, a total of 192 pairs fulfilling these requirements were available for analysis (Jarvik, Falek, Kallmann, & Lorge, in press). Despite the declining trend in intra-pair differences with advance into the senium, differences are smaller for one-egg than for two-egg pairs in all age groups.

Intellectual functions

Psychometric data on changes in intellectual functions during senescence show similar trends. There were 134 pairs who met the requirements of being white, literate, native born, non-institutionalized, and apparently free of mental and physical illness, and who had been tested when this study was first undertaken.

The test battery included four subtests of the Wechsler-Bellevue Intelligence Scale I (digit

TABLE 1. DISTRIBUTION OF 1019 PAIRS FORMED BY 1603 SENESCENT TWIN INDEX CASES.

	Monozygotic		Dizygotic		Opposite Sex	Unclassified		Total
	Male	Female	Male	Female		Male	Female	
Mental hospitals	18	30	28	49	94	24	37	280
Other hospitals	1	1	5	1	7	5	0	20
Homes for the aged	4	9	2	12	36	13	13	89
General population	93	105	79	121	158	32	42	630
Total	116	145	114	183	295	74	92	1019

TABLE 2. SURVIVAL TRENDS IN A SENESCENT POPULATION.

	Per cent survival by age					
	Age 60	Age 65	Age 70	Age 75	Age 80	Age 85
Males:						
General population[a]	100	87	71	52	33	16
One-egg	100	91	79	54	33	20
Two-egg, same sex	100	93	79	61	36	15
Opposite sex	100	93	85	67	41	17
Unclassified	100	90	77	60	33	6
Females:						
General population[a]	100	92	81	65	46	26
One-egg	100	96	88	74	46	26
Two-egg, same sex	100	96	90	77	57	31
Opposite sex	100	89	77	61	41	20
Unclassified	100	97	89	71	57	18

[a] White United States population.

TABLE 3. MEAN INTRA-PAIR DIFFERENCES IN LIFE SPAN OF 192 SENESCENT TWIN PAIRS OVER AGE 60.[a]

Age group of first deceased in years	Mean Intra-Pair Differences in Months				
	Male		Female		Opposite sex
	One-egg	Two-egg	One-egg	Two-egg	
60–64	113 (7)[b]	130 (2)	102 (3)	215 (5)	138 (8)
65–69	39 (8)	82 (11)	71 (6)	122 (4)	183 (3)
70–74	66 (13)	78 (6)	68 (7)	97 (6)	80 (7)
75–79	38 (4)	42 (9)	49 (9)	70 (13)	68 (5)
80+	35 (4)	42 (8)	36 (14)	48 (24)	68 (6)

[a] Both partners died of natural causes.
[b] Figures in parentheses refer to number of twin pairs.

symbol, block design, similarities, and digit span), List I of the Stanford-Binet (1916) Vocabulary Test, and a simple paper and pencil tapping test.

In 1955, retests were administered to 36 pairs and to seven single survivors after an interval of almost eight years. The retested group approximated that of the original test series with respect to sex and zygosity distribution (Feingold, 1950; Jarvik *et al.*, 1957). In both series the largest subgroup was that of the one-egg females, followed in order by one-egg males, two-egg females, and two-egg males.

The original and retest results have been arranged (Figure 1) in such a way that the mean raw scores of the 79 retested subjects can be compared with the mean scores of the total test population in 1947 as well as with their own 1947 mean scores. Mean retest scores for the same subjects are lower on all six tests of the battery, with statistically significant declines ($p \leq 0.01$) limited to performance tests.

In comparing original mean test scores of the retested population with those of the entire sample, one finds that survivors achieved higher (though not statistically significant) mean scores on all original tests. Such differences, while in need of confirmation, do suggest some measurable selectivity with respect to biological survival values.

Comparative intra-pair differences in test scores between monozygotic and dizygotic twin partners are shown in Figure 2. In the original test population significant differences were observed between the two zygosity groups at the 0.01 level of confidence for the vocabulary, digit symbol, block design, and tapping tests. While the retest series was numerically too small to demonstrate significant differences between the zygosity groups, with the exception of the digit span, mean intra-pair differences were greater in the two-egg than in the one-egg pairs.

Conclusions

In a study of 1603 white senescent twins residing in New York State with life spans of 60

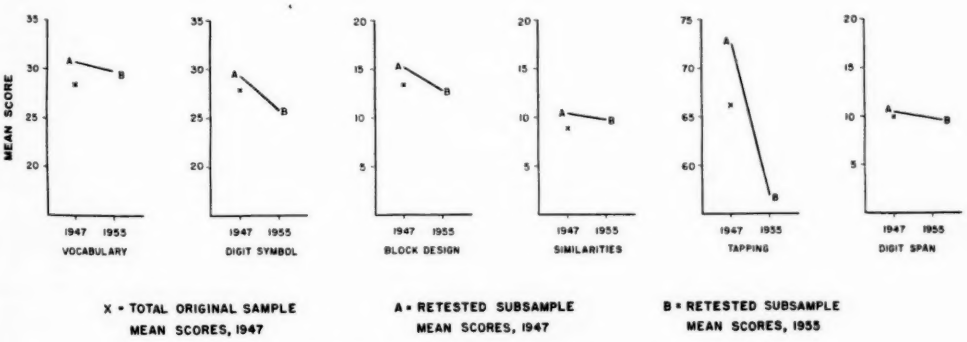

Fig. 1. Intellectual decline in senescence (longitudinal data).

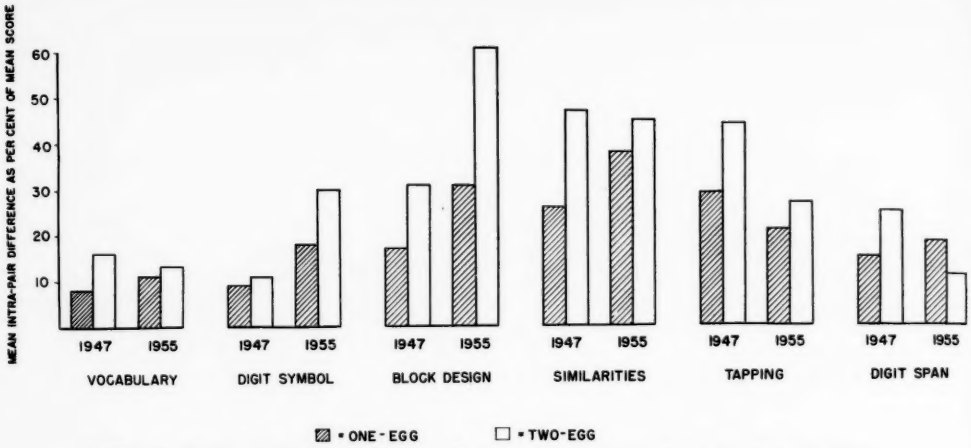

Fig. 2. Comparative psychometric performance of one-egg and two-egg twin partners.

years or more, the following results were obtained:

1. Survivorship in the twins was as high as that in the general population after age 60, lending further support to our working hypothesis that in a longitudinal study of this kind a sample of twins is representative of the total population.

2. Despite a consistent decline in intra-pair life span differences with increasing age, mean intra-pair differences in length of life remained smaller for one-egg than for two-egg twins of the same sex.

3. In the psychometric analysis (134 same-sex pairs were used for the original test series of whom 36 were retested eight years later), mean retest scores showed declines for all six subtests of the battery.

4. Mean intra-pair differences in test scores were larger for dizygotic than for monozygotic pairs at the time of the original test series and for five of the six subtests at the time of retest in 1955.

It may be concluded, therefore, that biological similarities between one-egg twins persist into the senescent period, confirming the influence of basic hereditary factors upon intellectual function as well as upon length of life.

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BOOK REVIEWS

Handbook of Aging and the Individual: Psychological and Biological Aspects. Edited by JAMES E. BIRREN. Chicago: University of Chicago Press, 1959. Pp. xii + 939. $12.50.

This monumental work, 939 pages in length, is the first of three volumes conceived and edited under the aegis of the Inter-University Training Institute in Social Gerontology. It has four major sections or sub-divisions respectively entitled Foundations of Research on Aging, Biological Bases of Aging, Aging in Environmental Settings, and Psychological Characteristics of Aging. It is obvious that a book of this kind cannot adequately be reviewed within a short space. The present comments pertain, therefore, only to Part Four, which alone spans over 400 pages.

Here one finds chapters on sensory functions by Weiss; perceptual processes by Braun; psychomotor performance by Welford; theories of learning and aging by Kay; age and learning-experimental studies by Jerome; intelligence and problem-solving by Jones; drives, expectancies, and emotions by Botwinick; the use of time and energy by Anderson; personality theory and aging by Riegel; and aging and life adjustment by Kuhlen. The authors have reviewed the literature carefully; have digested, summarized and systematized it nicely; and have given the reader an excellent conception as to both the present state of our knowledge and the types of vistas which lie ahead.

Since compendia tend to have their own peculiar strengths and weaknesses, comments of the following sort seem in order. First, the organization and coordination of topics treated is very good. The first three chapters of part four essentially cover S-R processes; the next four deal with "higher loops," or central or internal functions; and the final three view the organism globally and in its environment. Each chapter will stand alone; yet there is a logical sequence to the treatments and a minimum of duplications among them.

Second, contrary evidence and research needs are clearly identified. For example, Jones' excellent review clearly points up the discrepancy between results obtained in longitudinal and cross-sectional studies of the effects of age upon mental abilities. The writer finds himself not entirely in accord with the explanations offered, but applauds the attack upon a critical issue. Or, illustrating a direct statement of research needs, Braun says, "From a basic research point of view, many significant sensory phenomena have not been related to aging. In vision, these phenomena include light adaptation, saturation discrimination, after-images, brightness contrast, and color contrast, to mention a few."

Third, the true comprehensiveness of a compendium may always be questioned. In this instance the writer doubts that one tenth of the information found in the *Handbook* could be obtained from any other single source. It seems safe to say that a careful reading of a part of this single volume would bring one substantially up to date on the psychological aspects of gerontology.

Finally, a question arises as to the functions potentially to be served by the *Handbook*. Dr. Birren says, "It is intended for use by graduate students and professional and scientific specialists as a reference work." It will surely fulfill this intention. Hopefully, if universities in the future establish integrated departments of gerontology, the *Handbook* might even serve as a sort of interdisciplinary, graduate text. Meanwhile, it is a volume which will be rewarding to every serious student of aging.

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Retirement and Insurance Plans in American Colleges. BY WILLIAM C. GREENOUGH AND FRANCIS P. KING. New York: Columbia University Press, 1959. Pp. xvi + 480. $8.50.

This book, written jointly by the President and by the Research Officer of the Teachers Retirement and Annuity Association, is definitive, as of 1960, for the study of college retirement and health plans. It is designed primarily for the use of university and college administrators, trustees, and faculty members. Three hundred pages are devoted to a tabular presentation of data on retirement plans (including retirement ages) of about 1,000 American colleges and universities.

Of the 1,100 four-year institutions that responded to the inquiry, 85 per cent have retirement plans. Since many of the schools that did not respond do not have retirement plans, it would probably be fair to estimate that 76 per cent of four-year colleges and universities in the United States have retirement plans covering 91 per cent of college faculty in four-year institutions.

This book stresses the financial aspects of retirement plans. There is an objective discussion and evalution of the Federal Old Age and Survivors Insurance plan, of state plans for teachers and public employees, of Life Insurance Company plans, and of the Teachers Iusurance and Annuity Association plans. The TIAA-sponsored College Retirement Equities Fund is described in detail as a method of protection of retirement income against the dangers of monetary inflation.

The subject of health insurance is covered in two chapters, one dealing with basic hospital-surgical-medical insurance, mainly of the Blue Shield-Blue Cross type, and the other dealing with Major Medical Expense Insurance. This latter chapter describes the recent rapid growth of such plans for insurance against the high cost of major medical treatment, which is not provided by Blue Cross-Blue Shield plans. At the beginning of 1959 there were 154 institutions with major medical expense insurance, including 57 in the TIAA plan.

The Chapter on "Provisions of College Retirement Plans" devotes considerable space to the question of the age of retirement. The 1958 report of the Joint Committee of the American Association of University Professors and the Association of American Colleges is referred to with approval. This report favors a "fixed and relatively late retirement age," between 67 and 70. Sixty per cent of the colleges have 65 as their normal retirement age, but 80 percent of these permit extensions in individual cases, generally a year or two years at a time up to age 70. The important question here is what proportion of professors are actually given extensions

as compared with the proportion who would like to continue teaching after age 65. This question cannot be answered from the data given in this book.

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BOOKS RECEIVED

AXELROD, S. J. *Public Assistance Medical Care: Areas of Needed Research and an Annotated Bibliography.* Chicago: American Public Welfare Association, 1313 East 60th St., 1959. Pp. 63. $2.00. (paper)

CALIFORNIA. DEPT. OF PUBLIC HEALTH. *California's Older People—Their Health Problems.* 1959. Available from Malcolm H. Merrill, M. D., Director, 2151 Berkeley Way, Berkeley 4, Calif. Pp. 50. No price indicated. (paper)

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Section C

Organization Section
Index to Current Periodical Literature

VOLUME 15, SECTION C JULY, 1960 NUMBER 3

Reports from Foreign Correspondents

GERONTOLOGICAL ACTIVITIES IN FRANCE, 1957-1960

FRANÇOIS BOURLIÈRE

During these last three years, the study of aging has, at last, gained official recognition in French universities and official circles.

The first medical school to organize specialized courses of clinical gerontology has been the Faculty of Nancy, where R. Herbeuval has patiently but enthusiastically converted in a few years an almost medieval "hospice" for old people into an efficient geriatric hospital. All the participants of the Nancy-Vittel meeting last June have been able to see for themselves what has been realized with very little money. Herbeuval and his assistants can now extend their pioneer enterprise, and regular lectures on diseases of old age and their treatments are delivered to all medical students during the fourth year of their curriculum. It is to be hoped that a full geriatric clinic will be organized very soon.

In Paris, the building of the Gerontological Research Unit called Centre de Gérontologie Claude Bernard was completed in October, 1958, and work in the Unit started at once. Its official opening took place January 16, 1959, in the presence of numerous French officials and Prof. F. Verzár, who represented the European section of the Biological Research Committee of the International Association of Gerontology. The original grant which made this foundation possible was made by the Conseil Général de la Seine (Paris County Council) then under the chairmanship of Dr. J. A. Huet. The same body has since then extended its financial contribution and enabled the employment of 8 full-time research workers and laboratory assistants. Other workers are paid by the National Research Council and the National Institute of Health. Scientific direction is assumed by Dr. F. Bourlière. The main objective of this unit is the study of the ecology of human aging. Samples of healthy people are drawn at random from various socio-economic groups of the French population and persuaded to come to the Centre to be examined and tested. Experimental studies on animals continue to be made in the Department of Physiology of the Paris Medical School.

In June, 1959, a chair in Gerontology was created in the Medical Faculty of the University of Paris and conferred upon Dr. F. Bourlière. Research, not teaching, is its main objective, and the training of new workers in the fields of biological, psychological, and clinical gerontology is now being undertaken.

At the same time, the French Institute for Demographic Studies organized a Section of Ageing, which is now directed by Mr. P. Paillat, with the help of Dr. Biraben. The various demographic and economic problems raised by the aging of the French population are its main concern. In 1959, also, J. R. Tréanton, who has made the social aspects of aging his leading research objective, has been appointed "chef de travaux" in the Faculty of Letters and Human Sciences of Lille University.

This interest in gerontology, which is now growing in France, is well exemplified by the two international symposia which were organized during the last 12 months. A clinical meeting, sponsored by the European Section of the Clinical Research Committee of the IAG, took place in Nancy and Vittel from June 25 to June 28, 1959, under the chairmanship of R. Herbeuval. The reports presented and the proceedings of the discussions were published in the fifth volume (pp. 335-692) of the *Revue Française de Gérontologie*. The two themes which were discussed at length were the treatment of apoplexy and the degenerative diseases of the osteo-articular system.

An International Symposium on Psychological Ageing was held in Paris, from April 10 to April 16, 1960. Sponsored by the National Research Council (C.N.R.S.) and very efficiently organized by Madame S. Pacaud, this meeting was attended by 20 French and 11 foreign scientists. The more important original contributions presented on that occasion are mentioned below. All the reports and the summary of the discussions are being printed in book form, as volume 96 of the *Colloques Internationaux du Centre National de la Recherche Scientifique*.

Besides those two international symposia, clinical meetings have been organized recently in various French cities: Avignon, Bordeaux, Lyon, Marseille, and Montpellier.

Some Original French Contributions to the Field of Scientific Gerontology

It is beyond our purpose to list here all the gerontological papers which have been published in France during the last three years; we prefer to single out a few which are of more than local interest in the fields of biological, psychological, and social gerontology.

Biology of aging.—J. Lejeune and R. Turpin (1957) have confirmed that the frequency of male births tends to decrease with advancing paternal and maternal age in man.

The morphological age changes (from 20 to 90 years of age) in a random sample of the French population ($N = 364$) have been studied by S. Parot (1959), and F. Bourlière, S. Parot, and H. Pineau (1960); these findings are now being correlated with various physiological and psychological variables. The stature (standing height) lowers considerably, especially after 45 years of age. This diminution is mainly due to

a shortening of the trunk and the cervico-cephalic region; the limb length (= difference between standing height and sitting height) does not change very much with age. At the same time, a diminution of the biacromial breadth and an increase of the bi-iliac breadth can be observed. The acromioiliac index increases noticeably with age, while the thoracic index decreases considerably. At the same time, one notes a regular increase of the systolic blood pressure and a linear decrease of the vital capacity as people get older. All these changes are much more accentuated in women than in men.

Among other physiological age changes which have been carefully studied recently in France, the following ones seem to be the more important for gerontologists.

M. Burstein and J. Samaille (1958) have described a new and simple method of determination of β-lipoproteins in blood, which is now extensively used in France and other countries as a routine procedure. Such a method enabled them to study the variations of β-lipoproteins content of human serum with age, sex, and a great many pathological conditions. Although there exists an important inter-individual variability (quite probably due to variations in the diet), there is a regular increase with age of the serum β-lipoproteins in the French population. On the average, the values found are higher for men than for women.

The rate of uptake of radioactive iodine in 1357 healthy individuals of both sexes has been investigated by M. Tubiana and his co-workers (1958). I^{131} uptake has been found to decrease regularly with age in both sexes.

J. Warter, L. Asch, and C. Aron (1959) have studied the urinary excretion of thyroid-stimulating-hormone in 14 men and 16 women, ranging from 70 to 92 years of age, using M. Aron's method. The values found did not differ significantly from those of adult subjects. TSH content of pituitaries of 15 adults and 22 old people of both sexes has also been estimated, with the same method. Again no significant age difference was found between the two groups.

The amplitude of accommodation has been studied with Badal's optometer in 2137 individuals ranging from 10 to 86 years of age by F. Bourlière, M. Coumétou, and S. Pacaud (1960). Not only the range of accommodation but also the *punctum proximum* and the *punctum remotum* have been determined. If the median values of the *punctum proximum* decrease regularly till the age of 60, the median values of the *punctum remotum* increase until the age of 55.

The influence of age on the perception of sweet and salty tastes has been studied by F. Bourlière, H. Cendron, and A. Rapaport (1958) in 81 healthy persons of both sexes, ranging from 20 to 93 years of age. The thresholds of perception and recognition for sweet taste are much higher in older subjects than in younger ones. For salty tastes, only the threshold of perception seems to raise with age.

Age variations of the electroencephalogram and its reactivity to hyperventilation and photic stimulation have been investigated in 879 subjects, whose ages ranged from 30 to 89 years, by G. Verdeaux, J. Verdeaux, and J. Turmel (1960). A decrease of the alpha-frequency with age has been noted; at the same time, blocking is less and less adequate, hyperventilation becomes more and more active, theta rhythm increases, and the photic stimulation influences less the cerebral rhythm, but its action increases the irritative pattern.

The duration of sleep has been investigated in 380 healthy individuals of both sexes, whose ages varied from 30 to 80 years, by F. Clément and F. Bourlière (1960). From these preliminary results, it seems that the duration of sleep remains remarkably constant throughout life for people who never regularly use any narcotic; its average value in the sample studied was 7 hours 20 minutes. This duration is not much influenced by the sex of the individual, his intellectual and cultural background, and his intellectual activity. Twice as many women than men take narcotics regularly and the use of these drugs seems to increase as the subjects get older. This habit is less widespread among very physically active people (2%) than among sedentary individuals (20%).

Among the few experimental studies, three may be mentioned. N. P. Buu-Hoï and A. R. Ratsimamanga (1959) have found that an antioxydant, the nordihydroguaiaretic acid, mixed with the diet (20 mg. per Kg. of food), can extend the longevity of rats when given regularly during the whole lifespan of the animals. L. Binet, F. Bourlière, and R. Molimard (1959) have investigated the action of various embryonic extracts on the rate of regeneration of the liver and the compensatory hypertrophy of the remaining kidney after unilateral nephrectomy in rats of various ages (2 to 26 months old). The extract which contained the greatest amount of nucleoproteins and which was completely devoid of any kind of lipids was found to increase significantly the rate of the liver and kidney hypertrophy. F. Bourlière, H. Cendron, and B. Tesnière (1958) have compared in rats, aged from 16 to 34 months, the sparing action of various androgens and synthetic steroids on the nitrogen loss of animals temporarily maintained on a nitrogen-free diet. Testosterone propionate was found to be the most active in restraining nitrogen losses.

Psychology of aging.—Most of the original French contributions in this field have been summarized in the proceedings of the C.N.R.S. symposium held in April, 1960, to which the reader is referred for more details. We shall limit ourselves in this review to a few papers of general interest.

H. de Gobineau and R. Perron (1958), using a graphometric test of their own which permits an objective determination of handwriting level and shows a good correlation with the Wechsler-Bellevue scale ($r = 0.81$), have made a longitudinal study of 21 subjects and a cross-sectional study of 1291 other subjects. They have found that this index keeps growing till the age of 40 to 50 years and does not decline before 60. The higher the cultural and intellectual level, the later the decline.

S. Pacaud (1960) has made an extensive study of the intra-group variability of various intellectual and psychomotor performances, at various ages (20 to 55 years), in 4000 individuals belonging to a very homogeneous socio-economic group. She has found that intra-group variability does not change much with age for intellectual performances, while it increases regularly as the subjects get older for most psycho-motor performances. The level of instruction may also influence this intra-group variability and reduce somewhat the age differences.

F. Clément and F. Bourlière (1959) have compared

the performances of 282 subjects of both sexes, who were given Wechsler and Binois-Pichot vocabulary tests. In the upper cultural level better performances are observed around the age of 50, while in a lower cultural level the performance continues to improve up to the age of 70. The vocabulary differences between subjects of various cultural levels therefore tend to decrease with age.

Sociology of aging—M. Dupland (1959) has made a thorough and penetrating study of attitudes toward retirement and their motivations in a random sample of 95 primary school teachers she examined a few months before the cessation of their professional activities. Miss Dupland found that 55% feared that retirement would make them age more rapidly and that the adjustment to the new type of life depends greatly upon the pre-retirement conditions and attitudes of the individual. Teachers who cease their activities because they are compelled to do so as a result of the legal age limit are much more anxious and pessimistic than those who retire on a voluntary basis. Women, unmarried people of both sexes, people who did not make adequate material and financial preparation for their retirement, and people whose familial and social relations are poorly developed do not adjust themselves to the new situation as well as the others. The same individuals will be studied again next year and their changes of attitudes recorded.

S. Pacaud and M. O. Lahalle (1960) have studied attitudes after retirement in a sample of 108 individuals living in an old-age home in the suburbs of Paris. The influence of the past profession and of the state of health has been emphasized. There seem to exist certain definite links between psychosocial behavior and the biological and social factors studied.

J. R. Tréanton (1960) has made a study of the attitudes of 264 workers toward retirement problems. Poor health and fatigue were the principal reasons for the cessation from work in 50.5% of the cases, both in manual and white collar workers. If confirmed by a more extensive survey, such an incidence of physical conditions would greatly reduce, on the economic level, the favorable effects that could be expected in France from a postponement of the age of retirement.

P. Paillat and A. Sauvy (1960) have made a scholarly review of the historical changes of attitudes toward aged people and retirement problems in France during the last three centuries. Figures are also given which show how small are the avowed resources of a large part of the retired old people in France.

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GERONTOLOGY IN THE NETHERLANDS

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Since the last report on some gerontological activities in the Netherlands,* both research and old age care programs have been developed further. The Organization for Health Research (T.N.O.), formerly the National Health Research Council, continued its activities in biological and clinical research. At the Antonie van Leeuwenhoekhuis at Amsterdam, the emphasis was again on experimental investigations (11, 12), such as the gonadotropic effect of the adeno-hypophysis in old age on ovaries of purebred strains of mice, the condition of the endometrium of the uterus (for instance, hyperplasia was imitated through lifelong estrone administration; the effect of progesterone administration), the changes in old mouse adrenals, and the biology of the skin and hair-growth in mice and men, as influenced by endocrine factors. At the moment, the last-mentioned studies, which will include investigations of the preputial glands and of skin transplantations, are in progress. In various university and other laboratories more investigations (3, 5, 8, 17, 20) with respect to processes of aging are going on, such as biochemical, physiological, clinical, and nutritional studies of atherosclerosis (2, 21), Paget's disease, and senile osteoporosis. The latter studies, at present under the direction of Frenkel, are again T.N.O. activities. Such is also the case with the combined clinical, pathological, bio-

* *J. Gerontol., 13:* 453-454; 1958; see also *J. Gerontol., 11:* 213-214, 1956, and *J. Gerontol., 13,* suppl. 1: 67-91, 1958.

chemical, psychological, and sociological studies of the inmates of a large municipal home for the aged at Rotterdam, which will be completed this year. In the clinical investigations the same standard questionnaires are used as in the clinical studies of the male inmates of the Amsterdam municipal home for the aged and in the nation-wide survey of the health of the aged. The work in Amsterdam includes special clinical and biochemical examinations of the prostate, and there, as in Rotterdam, autopsies with emphasis on the processes of aging are performed. Moreover, at Amsterdam, a re-examination takes place after about two years. This whole project will be concluded in 1961.

Naturally, in many hospitals, more specific clinical investigations in elderly patients have been performed or are still under way, as can be seen, for instance, in the increased number of relevant articles in the medical periodicals (e.g., 9, 15) and other clinical publications.

Special mention should be made of a clinical study (7) of the health of 3009 apparently healthy people between 40 and 65 years of age in Amsterdam in which many previously unknown serious abnormalities were found.

Another large T.N.O., project in the field of psychology, is also nearing its final stage, i. e., the framing and standardizing of an intelligence test for aged and adult people under the direction of Snijders, at the Institute of Psychology, University of Groningen. After the completion of a test battery, pilot studies have been performed in some parts of the Netherlands, before a nation-wide representative sample of people between 12 and 88 years of age was examined. The chief investigator, Verhage, will publish his results this year. It may be added that close links were laid between these and the Rotterdam psychological studies, in which, however, various other tests are also used.

The hitherto largest T.N.O. investigation, the nation-wide survey of the medical, psychological, and social status of 3,149 people of 65 and over, with the help of 374 general practitioners, was finished successfully. A comprehensive report is to be published in English in 1960 (27). Some few specific data have already been published (24, 25).

A statistical study, partly subsidized by T.N.O., on the mortality of people over 50 years of age was completed and published. The author, Mulder (13), a general practitioner, studied in particular the differences in mortality between urban and rural areas. He found, among other things, that while the death rates for women are lower than for men, there is for the former no difference between these areas, but that for men mortality is highest in the towns. For many separate causes of death, analyses are made and explanations for any differences given.

In some other statistical investigations, as on the scientific value of data of health insurance groups (19) and on suicide, special attention was given to the aged.

In this connection it may be noted that with respect to the results of the 1960 population census, partly at the request of the Netherlands Society of Gerontology, the Central Bureau of Statistics will prepare more extensive data on the older population sections than ever before.

Social gerontological research, which was lagging behind, has received more attention during these last few years. In the last decade quite a number of local studies, mostly on the living conditions of the aged, have been performed, but only a few yielded data of general nation-wide importance (22, 26). Among these may be mentioned: the sociological study of 804 elderly people (over 55 years of age) in a part of Amsterdam (10), the survey on the living conditions of 6,400 aged men and women in Rotterdam (18), the survey (14) in a sample of 493 on the need for accommodation and care for the elderly in Sittard (a small industrial town of 28,000 inhabitants in the South of the Netherlands), the survey of the accommodations and care in the residential homes constructed after World War II (16), and the investigation of the opinion of the aged on accommodations planned for them (6).

Under the auspices of the National Committee (now the Netherlands Federation) for the Care of the Aged, Diederich studied the living conditions of 11,304 elderly people in small and middle-sized townships, thus performing for the first time in the Netherlands a more or less nation-wide socio-geographic old age survey (4).

Recently, closer coordination was established between the Netherlands Federation for the Care of the Aged, the Research Section of the Ministry of Social Work, and a number of sociological institutes. As a first result, a sociological, psychological, and medical study of the causes of loneliness and of the means to avoid it has been started in a number of aged people at Amsterdam. A second project, on the sociological implications of retirement, is in preparation, as are longitudinal and other studies.

The Netherlands Society of Gerontology (23) does its share in promoting all these research activities. It has by now three sections: clinical, social research, and biological, which all meet separately several times during the year and occasionally with other societies. Besides, there are at least three general meetings, mostly in modern old age homes, every year. Membership is nearing 300. Members attend at nearly all seminars, colloquia, study groups, conferences, and congresses on gerontology or geriatrics in Western Europe or where gerontological aspects are discussed. On the other hand, many foreign gerontologists visit the Netherlands.

The care of the aged has been further considerably improved, among other provisions, through the General Old Age Law, which provides every aged citizen with a state pension (for which premiums are paid by employers and employees); a law providing health insurance coverage at low premiums for aged people with incomes below a certain level (about two-thirds of the approximately one million people 65 and over are thus insured); extension of the regulations regarding the employment of people to help the aged in their homes.

With respect to housing, much progress has been made. In the years 1951-1958, 172 homes for the aged with 14,682 beds and 10,051 special small houses with 21,686 beds have been built. Emphasis is on building the latter category of accommodation. More and more a number of such homes are grouped around a central home, which may provide certain facilities, such as hot meals. Three important studies (1) on all aspects of housing for the aged have been published by the Bouwcentrum (International Center for Studies on Building).

About one-third of the male population aged 65 and over is still at work. At some places organizations

have been established to provide part-time activities for pensioners. Leisure time activities for the elderly have expanded greatly; at the moment, for instance, more than 1,500 clubs for old people exist, and the number is still increasing.

Health care for the aged receives more attention than ever; rehabilitation procedures have been introduced in many nursing homes. With regard to training of medical and nursing personnel in charge of elderly people, the Netherlands Society for Gerontology and the Netherlands Federation for the Care of the Aged have worked out detailed programs. A uniform training scheme for lower echelon personnel has been in effect for several years, and about 600 women have obtained the official diploma for their training in helping the inmates in old age homes.

This short review may indicate that the so-called problems of aging and old age receive much attention in the Netherlands, both in terms of research and actual care.

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ITALIAN CONTRIBUTIONS TO GERONTOLOGY, 1957-1960

GIORGIO MARS

Italy organized the Fourth International Congress of Gerontology, held at Merano and Venice from the 14th to the 21st of July, 1957, and attended by more than a thousand scientists from many countries. The enthusiastic and learned promoter, Professor Enrico Greppi, was on this occasion elected President of the International Association of Gerontology. The successful results of this scientific event have been summed up in the 4 volumes of the Proceedings.

In April, 1958, the National Institute of Italian Pensioners organized a meeting in Rome for the consideration of occlusive arterial diseases of the limbs in old age: the etio-pathogenical, morphological, semeiological, clinical, and therapeutical aspects of this problem were discussed by Professors Corsi, Cavallero, Strano, De Giuli, Condorelli, Ricci, Malan, and Provenzale, and Dr. Scarzelli dealt with the subject of parallelism between peripheral and cerebral arteriopathic conditions of senescence.

In December, 1958, the Italian Society of Gerontology and Geriatrics held its Seventh National Congress in Genoa. The subjects reported upon were: the respiratory system in old age, with particular reference to the various tests of respiratory function (Daddi and Fazio), pulmonary emphysema (Campanacci and Gunella), and pulmonary heart disease of the elderly (Volta); the senile larynx (Ferreri), and cerebral vascular diseases and their outcome, seen as a geriatric problem (Fazio, Cavalieri, and Farneti).

The Ganassini Gerontology Prize was awarded to the monograph, Arterial Hypertension in Old Age, by Beulcke, Mars, and Morpurgo.

The 12th of April, 1959, was proclaimed National Day of the Aged by the Italian Government; every year at this time cultural and social events will be organized for the benefit of old people.

An interesting symposium, dealing with nicotinic acid and its application in the geriatric field, took place

in Florence in July, 1959, and was attended by Professors Panuccio, Scarselli, Becattini, Antonini, Scardigli, and Guidi.

In October, 1959, the Eighth National Congress on Gerontology and Geriatrics was held in Rome. Senile diabetes was discussed by Professors Greppi, Adezati, Antonini, and Signorelli, who examined this condition from the various pathogenical, morphological, and clinical angles. Professors Bietti and Rubino, on the other hand, considered opthalmological problems of senescence, with particular reference to vascular symptoms of the eye in old age.

The Italian Association of Gerontology (AGEI) met in Milan in February, 1960, for the discussion of questions of a social and constructive nature; these comprised, among others, the relationship between aging and environment.

In March, 1960, examinations were held, for the first time in Italy, to enable candidates to qualify for a recognized university degree in gerontology and geriatrics; 9 candidates were successful.

Also in March, an Italian delegation under the leadership of Professor Greppi went to Roumania in response to an official invitation from the Roumanian Government in order to inspect the Institutes of Gerontology and Geriatrics in that country.

The regional sections of the Italian Gerontological Society have also carried out intensive scientific work during the last three years; particularly noteworthy are the following: a refresher course on gerontology held in Trieste in 1959; a comprehensive discussion which took place in the same year at Bologna, dealing with the various problems arising from senile cardiopathic conditions, as well as the important papers on the morphology and physiopathology of the suprarenal glands, given at Leghorn by Professors Greppi and Giampalmo.

The Italian Gerontological Society is now making preparations to participate, by sending delegates and scientific contributions, to the Fifth Congress of the International Association of Gerontology, which, as is already known, is to be held at San Francisco from the 7th to the 12th of August, 1960.

REPORT ON GERONTOLOGICAL TOPICS FROM IRELAND

JOHN F. FLEETWOOD

With more than 10% of the population over 65 years of age, the population of Ireland is already an aged one. In common with other countries, therapeutical discoveries are keeping more old people alive longer, but late infertile marriages and a high emigration rate among young people are the major factors in determining the age group distribution of the population. There is a growing awareness of the urgency of this social problem, but until the two elements mentioned have been dealt with, there is little hope of improving the situation. Consequently, most of the advances made have been in the field of social geriatrics rather than of laboratory or clinical gerontology.

The Irish Red Cross Society has been in the forefront of the efforts to secure better conditions for old people for many years and encourages all units to take an interest in the welfare of old people in their districts. They visit the aged in their homes, help them with shopping and cleaning, visit friendless old people in the County Homes, and arrange parties at Christmas and outings in the summer. In Dublin there are 12 organized groups in the city and suburbs, which can be called upon for duties, such as home-visiting, preparing a room for an old man or woman returning from the hospital, and running a social club. One group in Dublin has its own trained nurse and home-help employed especially for old people living alone, and they have cooperated with the Social Service (Tenements) Company of Dublin University in starting a small home for old men, women, and married couples. The aim of the Society is to have all units participating in this work, which not only benefits the old people but also provides a valuable peace-time training for Red Cross personnel.

In recent years, St. Kevin's Hospital, administered by the Dublin Board of Assistance, a statutory body, has developed an up-to-date Geriatric Unit in modern buildings situated on the grounds of the Hospital, having full access to all the general hospital facilities and services. It consists, basically, of an Active Therapy and Rehabilitation Hospital (150 beds) and a Long-stay Annex of 146 beds. In addition, there are two Residential Homes. One, St. Clare's, (100 beds) for frail, ambulant females, is located just outside the city; the other, Bru Chaoimhin, for infirm men (236 beds) and women (103 beds) is situated in the city. The admissions to the 150-bed (50 males, 100 females) Active Hospital during the year 1959 totalled 873, of which 509 were discharged, 159 died, and 157 were transferred to Long-stay accommodation. In addition to the medical and nursing staffs, there are two physiotherapists, an occupational therapist, a chiropodist, and an almoner, as well as the part-time services of a speech therapist. Admissions are usually received directly from the patient's own home, but patients are accepted from elsewhere in St. Kevin's Hospital and to a limited extent from other Dublin hospitals.

The occupants of the Residential Homes practically all come from St. Kevin's Hospital, but not necessarily via the Geriatric Unit. Each is under the charge of a matron, and every effort is made to provide recreational activities as well as a high standard of care for the residents.

In the rural areas, the problem of old people is not so acute as it is in the city, so that statutory and voluntary social developments have been less advanced. For many years, the County Homes (formerly the Workhouses) gave a minimum of service to old people, in common with the mildly demented, the handicapped, waifs, and strays generally. The standards of these homes have now been immensely improved. At the same time many old people still think of them as the Workhouse and are reluctant to seek shelter therein except as a last resort. This attitude is slowly disappearing as the homes prove their value.

The most important recent function of the Irish

Gerontological Society was the holding of a symposium, Problem of an Ageing Population, attended by physicians and ancillaries from all parts of the country. Among the speakers were Dr. William Hobson, Chief of the Education and Training Section of the W.H.O. Regional Office for Europe, who introduced the subject as a worldwide one, and Dr. Per From Hansen, of the Glostrup County Hospital, Denmark, who showed what could be done in a country comparable to Ireland in size and population.

In Northern Ireland rather more statutory services are available to old people than in the Irish Republic. The recently opened Geriatric Unit in the City Hospital in Belfast marked the culmination of some 10 years of hard work by G. Adams and his staff, while in the Braid Valley Hospital at Ballymena an old Workhouse wing has been converted into a modern hospital for geriatric patients.

The mobile physiotherapy unit operating in Belfast has proved its value in the home rehabilitation of old people. It is noted in reports from this service that intelligent cooperation by patients and their relatives is essential to its success.

In general one may say that in Ireland as elsewhere there is an increased social and medical awareness of the impact of aging on the population, and it is probable that this awareness will lead to increasing voluntary and statutory services in the future.

GERONTOLOGICAL ACTIVITIES IN DENMARK

TORBEN GEILL

The Danish Gerontological Society during the last few years has held meetings on gerontological problems (geriatric surgery, neurology, atheromatosis) in conjunction with other Danish scientific societies. At the last meeting, April 9, 1960, problems of social medicine were discussed. R. Friedberg and H. Hamtoft reported studies carried out by the Danish National Health Service. From a sampling survey concerning about 100,000 persons in Denmark, social conditions (such as housing, occupation, activities, hobbies, religious life, entertainments) were recorded. Further studies demonstrated the morbidity of elderly people, especially the occurrence of cancer and diseases of the heart, nervous system, and urinary tract. The material seems very valuable for physicians, hospital administrators, and the Public Health Service personnel. P. Milhøj discussed the activity of the new Institute for Social Research, which is under the guidance of the Ministry of Social Affairs. Statistical studies concerning elderly people will soon be published, including data on 1) income, savings, and expenditures, 2) retirement age from active work, 3) contact with family and community, 4) housing problems, and 5) health conditions.

In the following paragraphs are listed the investigations in the field of gerontology which have been published in the last three years.

M. Dyrbye studied the content and the metabolism of acid mucopolysaccharides in the human arterial wall, especially in regard to the changes related to aging and atherosclerosis. The author concludes that the acid mucopolysaccharides of the arterial wall play a role, perhaps essential, for age changes and especially for the development of atherosclerosis. The character and mechanism of the mentioned changes are still obscure.

Studies on the serum transaminases were carried out by P. Ollendorff. In patients between ages of 61 and 93 the serum glutamic acid-oxalacetic acid-transaminase (SGOT) and the serum glutamic acid-pyruvic acid-transaminase (SGPT) activity were investigated. It is concluded that it is unnecessary to determine SGPT in addition to SGOT and that transaminase investigations in elderly individuals render so many false positive reactions that a positive result is only of limited value.

H. Olesen reported two cases of typical macroglobulinemia in an 84-year-old-man and a 79-year-old woman. In the first case, a cancer of the prostate and chronic pyelonephritis were present. The sedimentation rate was found to be low on account of the presence of cryoglobulins. In the second case the only symptom was a continuous rise in the sedimentation rate.

Treatment of coronary sclerosis and coronary thrombosis was discussed by T. Geill, who gave a short review of the various new theories concerning the causation of atheromatosis, with special reference to disturbances in the metabolism of cholesterol, disturbances in blood coagulation, and fibrinolysis together with hypertension. A lowering of the cholesterol level in the blood is of great importance in patients with elevated cholesterol values. In the first place, animal fats in the food should be substituted by vegetable oils with high content of unsaturated fatty acids. According to Faber and Geill, two to three years' treatment with heparin did not lead to any change in atheromatosis in the aorta, in the serum-cholesterol level, or in the length of life of the patients concerned. The use of the so-called lipolytic substances is extremely erratic. In certain cases of hypercholesterolemia, however, a significant fall in serum-cholesterol may be seen following oral administration of lecithin or of a combination of choline, inositol, and polysorbate. The value of anticoagulants in the treatment of coronary thrombosis has been demonstrated, especially on the basis of the most recent results of long-term treatment in Norway and Denmark. The effect on persons over 60 years old seems doubtful. A case was reported of a 51-year-old man who was completely disabled by angina pectoris but who, after an operation using Beck's method, was able to return to full-time work.

T. Geill, E. Lund, and S. Vedsø studied the influence of a low fat diet rich in soybean oil on the serum cholesterol. The oil was given mainly as a margarine in which about 65% of the fat consisted of unhydrogenated soybean oil. In addition, a soybean milk prepared as a soybean emulsion in skimmed milk was used. The mean value of the serum cholesterol before treatment showed 232 mg./100 ml. in 24 women and 175 mg./100 ml. in 18 men, 62-94 years of age. The minimal serum cholesterol level was observed in both

groups following 6 weeks of treatment, and the reduction was 18.5% and 15.4%, respectively. When the special diet was changed to free diet, the serum cholesterol level rose to the values of the control period after a few weeks.

In order to investigate the influence of the fat content of the food on the formation of thrombi and emboli, T. Geill, P. From Hansen, and E. Lund treated a group of 133 hospital patients aged 65-90 years with a diet in which butterfat, margarine, and lard were replaced by vegetable oils (unhydrogenated corn oil and soybean oil). The daily intake of vegetable oils was about 40 Gm., or half the total fats. The time of treatment of the 133 patients ranged up to 17 months (average 4.7 months), representing a total of 52½ years. For comparison, a control group of the same size and composition, who received an ordinary hospital diet containing about 80 Gm. of animal fats (including 40 Gm. butterfat, margarine, and lard), was used. The occurrence of thrombosis and embolism in both groups was diagnosed clincally and post-mortem. In the treated group only 4 cases of thrombo-embolism were observed, in the control group 15 cases. The difference in the occurrence of thrombosis in the two groups of patients is statistically significant and cannot be interpreted in terms of variations in age, weight, and blood pressure in the groups.

The occurrence of hypertrophy of the prostate was found by E. Lund in half of the patients in a geriatric hospital. In 84% of the patients with prostatic hypertrophy, there was an infection of the urinary tract, and in 10% the serum creatinin was elevated. In 16 cases (13%) prostatectomy was carried out with good results in 11 of the cases. Genito-urinary disturbances in old age were studied by T. Geill. A steady reduction in renal function with advancing years in normal subjects was noted. This impairment is often aggravated by infection and obstruction. The dangers of electrolyte imbalance due to prolonged used of diuretics was discussed, together with some of the nutritional defects resulting from chronic renal impairment. The importance of investigating and treating specific diseases of the urinary tract before commencing rehabilitation therapy was emphasized. Among non-specific treatments, cystometry and administration of male hormone in elderly incontinent women have been found particularly effective. Anemia in pyelonephritis usually is refractory to simple iron medication orally or parenterally but responds to combined administration of iron and cobalt (20 mg. three times daily). E. Hansen and H. Gormsen studied the macrocytic anemias in old age. Hemoglobin percentage below 90 in men, below 85 in women, and color index above 1.20 in both sexes must be considered pathological in old age. In the marrow smears abnormally large erythroblasts (macroblasts) were often found. Morphologically fairly equal transitions seem to exist between normochromic, macrocytic, and pernicious anemias.

Psychology of old people and psychoses in old age were discussed by T. Geill. Delirious reactions are often a sequel of dehydration. Treatment of mental disorders with chlorpromazine has been very successful. A case of cirrhosis of the liver after use of this drug is reported.

Surgery in the senium was the main topic of a meeting of the Danish Surgical Society. T. Geill commented on organ functions in old age. In extensive material obtained at autopsy from people in the age range 70-90 years, 90.4% showed atherosclerosis of the coronary arteries and 69.5% had changes in their myocardium (fibrosis and sequels after infarctions in 40.9% and hypertrophy in 28.6%). Special reference should also be made to reduced kidney function in old age. Furthermore, a high percentage of patients in geriatric departments suffer from pyelonephritis with disturbed kidney function. P. From Hansen and T. Geill reported results from De Gamles By (Geriatric Department of Copenhagen). In 1952-1956, 266 patients were sent to the surgical departments for examination and treatment. Of these 174 underwent surgery. Primary surgery mortality was high (21%). Practically all patients with hernia should be operated on in time in order to prevent incarceration. A large statistical study from Bispebjerg Hospital, Copenhagen, by E. Amdrup, E. Halkier, K. Køster, P. Sønder, and F. Zachariae showed that mortality among 3,146 patients over 70 years of age who had undergone surgery was 12%. The authors summarized the results from different clinical groups: hernias, diseases of the liver, biliary tract, and pancreas, ulcers and other benign diseases of the esophagus, stomach, and duodenum, cancer of the stomach and intestine, abdominal emergencies, diseases of the urinary tract, gynecological disorders, vascular lesions in lower limbs, and traumatic lesions.

M. Felbo reported a large study concerning the relationship between physical conditions of the limbs of 65- and 70-year-old natives of the Danish island of Bornholm and their capacities for work. The reason and time of retirement and the reaction to retirement were evaluated.

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INDEX TO CURRENT PERIODICAL LITERATURE

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National Institutes of Health

THE SUBJECT categories are those in *A Classified Bibliography of Gerontology and Geriatrics* by Nathan W. Shock published by Stanford University Press, Stanford, California (1951). Only major headings are used and the Roman numerals correspond to those given in the bibliography. In so far as possible, references are classified according to organ systems. Thus, most of the material on Geriatrics will be found under the organ system involved in the disease. Cross references are indicated by number at the end of each section. When available, abstract references are given *(B. A.—Biological Abstracts, P. A.—Psychological Abstracts,* and *P. I.—Population Index).* Abbreviations for journals are those used in *A World List of Scientific Periodicals Published in the years 1900-1933, 2nd Edition.* For journals not listed, abbreviations were devised according to the general rules used in the above source. It is impossible to cover all journals and list all papers concerned with aging and the aged. Authors and publishers are requested to call attention to publications or to send reprints to the Gerontology Branch, Baltimore City Hospitals, Baltimore 24, Maryland. The assistance of the Forest Park Foundation, Peoria, Illinois, in the preparation of these materials is gratefully acknowledged.

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(allergy, anoxia, anesthesia, anthropometry, drugs, exercise, immunity, sleep, and temperature regulation)

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